Exposure Assessment Framework for Materials Selection in Consumer Electronic Products

Monty Liong, Ph.D.
June 12, 2019

IEEE

PSES
Product Safety Engineering Society

Silicon Valley
Chapter Meeting

Wearable Technologies

Earbuds

Watches/Fitness Tracker

Baby Monitor

Virtual Reality Technology

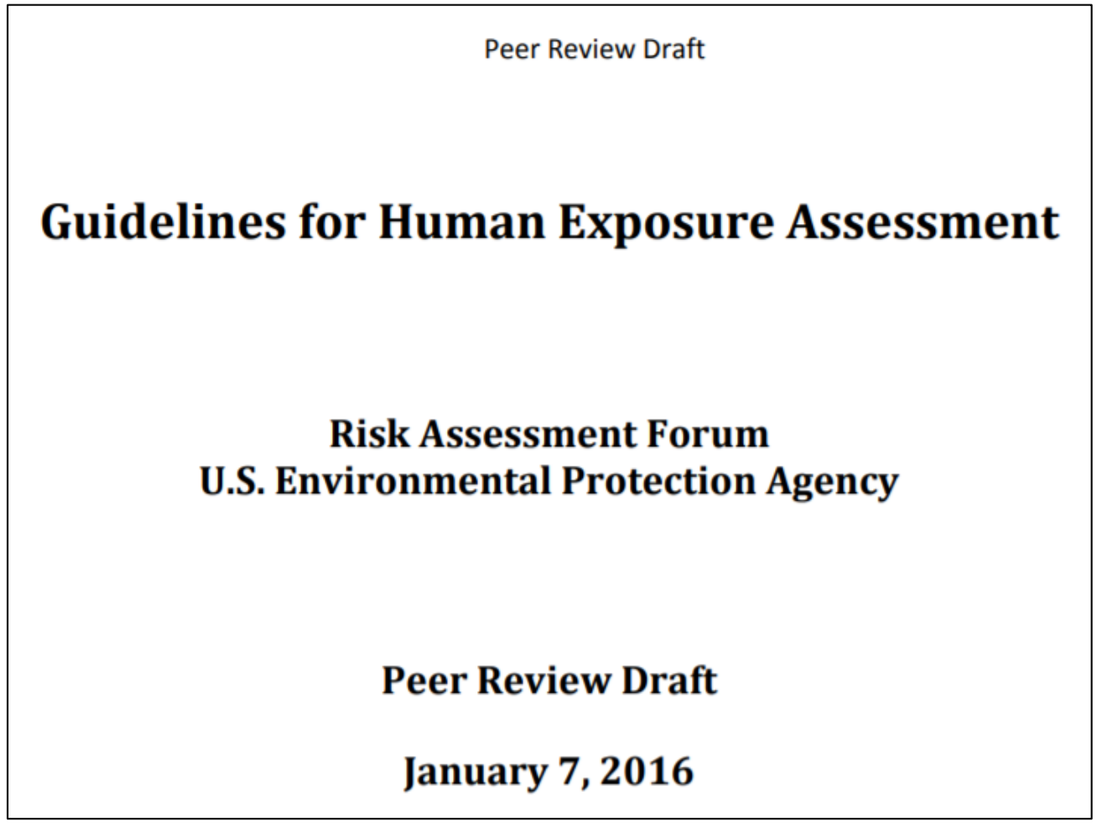
- The use of exposure assessment methodologies is crucial in materials selection for wearable technologies, particularly those involving long-term dermal contact
- The tiered exposure assessment described in this talk can be extended to the materials selection for various types of consumer products

https://assets.pcmag.com/media/images/465870-owlet-smart-sock-2-baby-monitor.jpg?width=333&height=245
https://contestimg.wish.com/api/webimage/5b99fda80fc3e348d8f3a466-large.jpg?cache_buster=3d9e04d7cb81c596c621be602e8142e8
https://images-na.ssl-images-amazon.com/images/I/61KWgg2zt0L._SL1001_.jpg
https://cnet1.cbsistatic.com/img/GYD4ueFYYUn397ot26qHbsx5tc8=/2018/04/04/6a6aaa42-2e21-43f4-abf0-27480949c6ee/sandboxvr-01.jpg

Outline

- Wearable technologies
- Human exposure assessment framework
- Regulatory compliance
  - RoHS, SVHC, Prop 65
- Dermal health effects
  - Moisture-associated skin damage, irritation, sensitization
- ISO 10993 biocompatibility evaluation
- Example Project #1: automobile interiors
- Example Project #2: exposure assessment of wearables
- Example Project #3: bisphenol A in Prop 65
- Example Project #4: release of new products

EPA Guidelines for Human Exposure Assessment


Peer Review Draft

Guidelines for Human Exposure Assessment

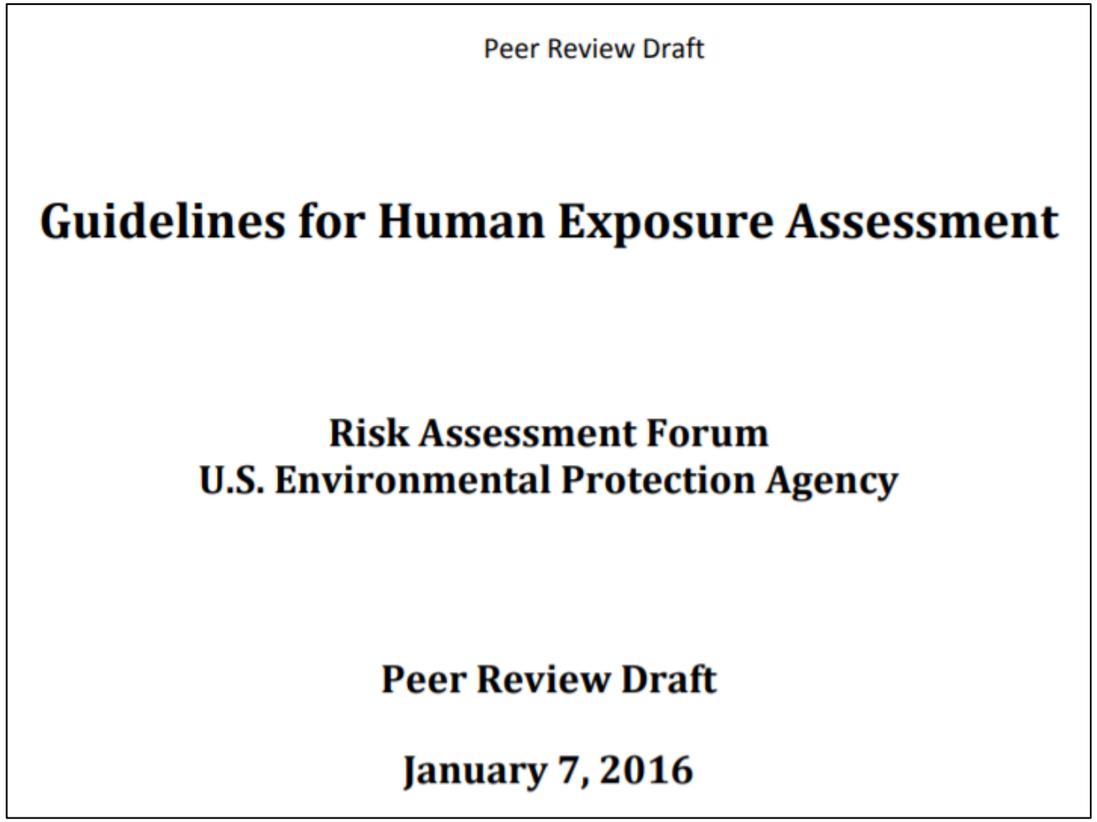
Risk Assessment Forum
U.S. Environmental Protection Agency

Peer Review Draft

January 7, 2016

- **Hazard identification**: identifies adverse effects (e.g., irritation, cancer) that might occur from exposure to a chemical
- **Dose-response assessment**: estimates the toxicity of the chemical by evaluating the quantitative relationship between exposure/dose and response (e.g., animal toxicity tests)
- **Exposure assessment**: estimates exposure to the chemical(s) of concern
- **Risk characterization**: estimates the potential for adverse effects resulting from a human exposure

Human Exposure Assessment Framework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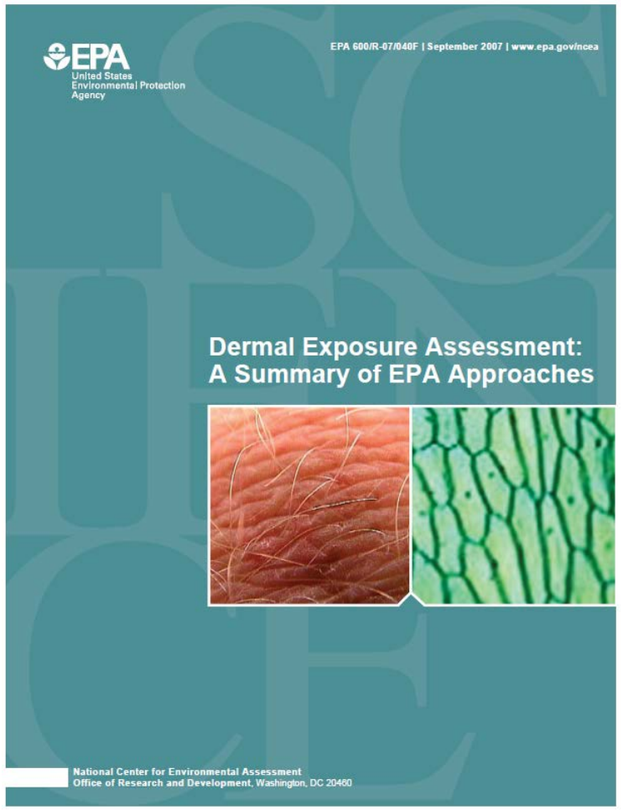
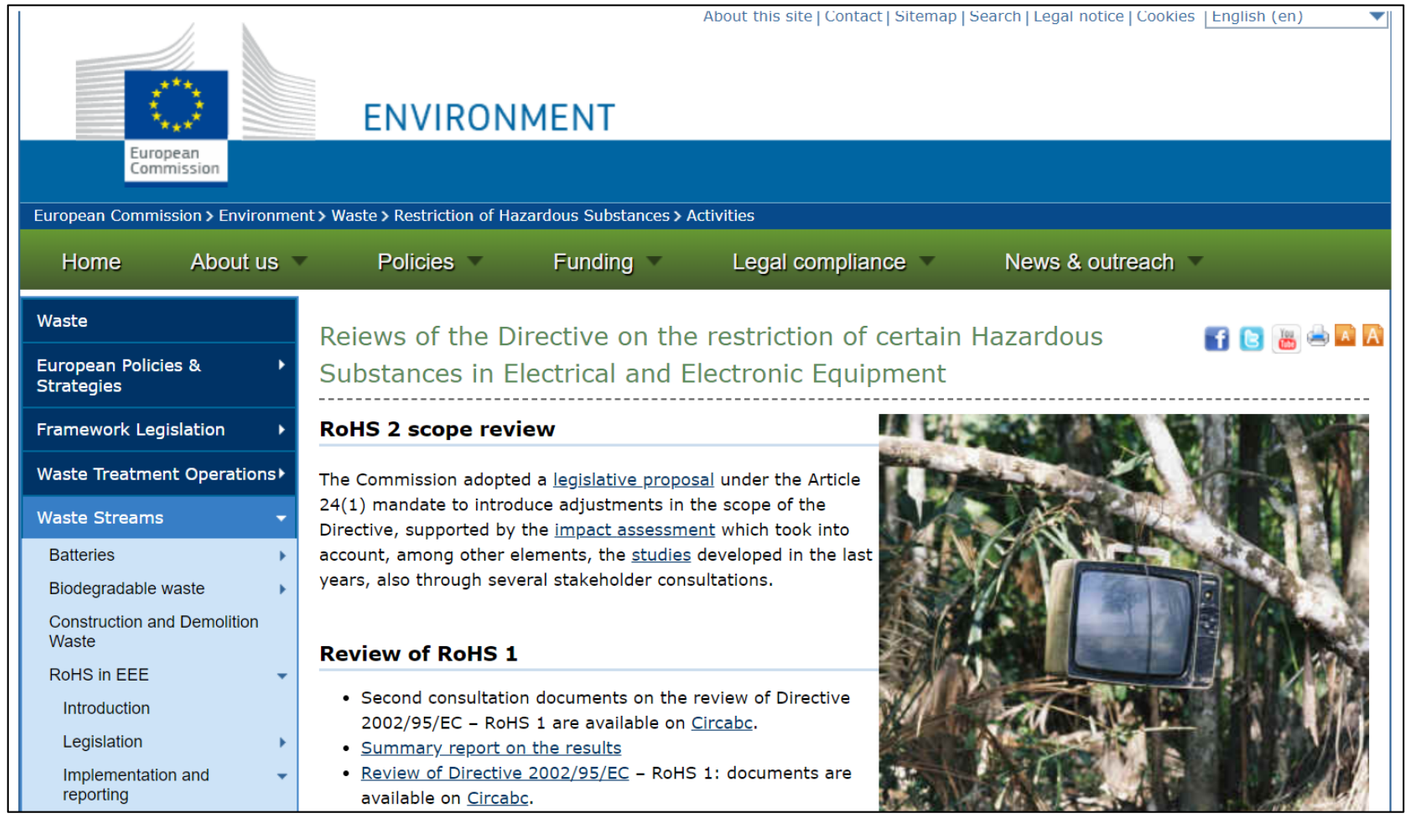


- Identification and quantification of chemical(s) of interest present in the product
- Quantitative evaluation of the different pathways where consumers are potentially exposed to the chemical(s) of interest from standard use of the product
- Determination of the potential human health risk from these exposures

Regulatory Compliance

RoHS Compliance



- Testing for Restriction of Hazardous Substances Directive 2002/95/EC (RoHS) and RoHS 2 directive (2011/65/EU) compliance:
  - Cadmium
  - Lead
  - Mercury
  - Hexavalent chromium
  - Polybrominated diphenyl ethers (PBDEs)
  - Polybrominated biphenyls (PBBs)
  - Certain phthalates
- Testing for RoHS compliance is to address environmental and health concerns
  - Not necessarily for dermal irritation or sensitization

Example RoHS Test Reports

SGS

Test Report No. SHAEC1721681606 Date: 24 Oct 2017 Page 2 of 12

Test Results :

Test Part Description :

Specimen No.	SGS Sample ID	Description
SN1	SHA17-216816.006	Transparent glass

Remarks :

(1) 1 mg/kg = 0.0001%
(2) RL = Report Limit
(3) ND = Not Detected (< RL)
(4) "-" = Not Regulated

RoHS Directive (EU) 2015/863 amending Annex II to Directive 2011/65/EU

Test Method : With reference to IEC 62321-4:2013, IEC62321-5:2013, IEC62321-7-2:2017 , IEC 62321-6:2015 and IEC62321-8:2017, analyzed by ICP-OES ,AAS, UV-Vis and GC-MS .

Test Item(s)	Limit	Unit	MDL	*006*
Cadmium (Cd)	100	mg/kg	2	ND
Lead (Pb)	1000	mg/kg	2	ND
Mercury (Hg)	1000	mg/kg	2	ND
Hexavalent Chromium (Cr(VI))	1000	mg/kg	8	ND
Sum of PBBs	1000	mg/kg	-	ND
Monobromobiphenyl	-	mg/kg	5	ND
Dibromobiphenyl	-	mg/kg	5	ND
Tribromobiphenyl	-	mg/kg	5	ND
Tetrabromobiphenyl	-	mg/kg	5	ND
Pentabromobiphenyl	-	mg/kg	5	ND
Hexabromobiphenyl	-	mg/kg	5	ND
Heptabromobiphenyl	-	mg/kg	5	ND
Octabromobiphenyl	-	mg/kg	5	ND
Nonabromobiphenyl	-	mg/kg	5	ND
Decabromobiphenyl	-	mg/kg	5	ND
Sum of PBDEs	1000	mg/kg	-	ND
Monobromodiphenyl ether	-	mg/kg	5	ND
Dibromodiphenyl ether	-	mg/kg	5	ND
Tribromodiphenyl ether	-	mg/kg	5	ND
Tetrabromodiphenyl ether	-	mg/kg	5	ND

SGS

Test Report No. SHAEC1721681606 Date: 24 Oct 2017 Page 3 of 12

Test Item(s)	Limit	Unit	MDL	*006*
Pentabromodiphenyl ether	-	mg/kg	5	ND
Hexabromodiphenyl ether	-	mg/kg	5	ND
Heptabromodiphenyl ether	-	mg/kg	5	ND
Octabromodiphenyl ether	-	mg/kg	5	ND
Nonabromodiphenyl ether	-	mg/kg	5	ND
Decabromodiphenyl ether	-	mg/kg	5	ND
Di-butyl Phthalate (DBP)	1000	mg/kg	50	ND
Benzyl Butyl Phthalate (BBP)	1000	mg/kg	50	ND
Di-2-Ethyl Hexyl Phthalate (DEHP)	1000	mg/kg	50	ND
Diisobutyl Phthalates (DIBP)	1000	mg/kg	50	ND

Notes :

(1) The maximum permissible limit is quoted from RoHS Directive (EU) 2015/863. IEC 62321 series is equivalent to EN 62321 series http://www.cenelec.eu/dyn/www/f?p=104:30:1742232870351101::::FSP_ORG_ID,FSP_LANG_ID:1258637,25
(2) On 4 June 2015, Commission Directive (EU) 2015/863 was published in the Official Journal of the European Union (OJEU) to include the phthalates BBP, DBP, DEHP and DIBP into ANNEX II of the Rohs Recast Directive. The new law restricts each phthalate to no more than 0.1% in each homogeneous material of an electrical product.
(3) The restriction of DEHP, BBP, DBP and DIBP shall apply to medical devices, including in vitro medical devices, and monitoring and control instruments, including industrial monitoring and control instruments, from 22 July 2021.
(4) The restriction of DEHP, BBP, DBP and DIBP shall not apply to cables or spare parts for the repair, the reuse, the updating of functionalities or upgrading of capacity of EEE placed on the market before 22 July 2019, and of medical devices, including in vitro medical devices, and monitoring and control instruments, including industrial monitoring and control instruments, placed on the market before 22 July 2021.
(5) The restriction of DEHP, BBP and DBP shall not apply to toys which are already subject to the restriction of DEHP, BBP and DBP through entry 51 of Annex XVII to Regulation (EC) No 1907/2006.

https://www.schott.com/d/advanced_optics/b9f8c939-39b3-428c-932c-8b867ffbb998/D263M_2017_10_24_ROHS10_ELEMENTS_ASBESTOS_PFOA_PFOS.PDF?tenant=ao-cert

ECHA REACH SVHC List

- Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH): 2006 European Union regulation
  - Production and use of chemical substances
  - Potential impacts on both human health and the environment

- 197 substances in REACH “Substances of very high concern" (SVHC) list (as of June 2019)
  - Includes certain phthalates, lead, perfluorooctanoic acid (PFOA)

Example Test Report for REACH SVHC

SGS

Test Report No. SHAEC1820866108 Date: 19 Sep 2018 Page 1 of 18

(SVHC)

SCHOTT AG, ADVANCED OPTICS
HATTENBERG STRASSE 10, D-55122 MAINZ

The following sample(s) was/were submitted and identified on behalf of the clients as : B270i

SGS Job No. :	SP18-031531 - SUZ
Lot No. :	2911956
Date of Sample Received :	13 Sep 2018
Testing Period :	13 Sep 2018 - 19 Sep 2018
Test Requested :	As requested by client, SVHC screening is performed according to: (i) One hundred and ninety one (191) substances in the Candidate List of Substances of Very High Concern (SVHC) for authorization published by European Chemicals Agency (ECHA) on and before Jun 27, 2018 regarding Regulation (EC) No 1907/2006 concerning the REACH.
Test Results :	Please refer to next page(s).

Summary :

According to the specified scope and evaluation screening, the test results of SVHC are ≤ 0.1% (w/w) in the submitted sample.	PASS

- SVHC screening performed by various test labs
- Analysis includes various chromatography and mass spectrometry techniques to analyze for metals and organic compounds

https://www.schott.com/d/advanced_optics/4bdffce0-e75b-43e9-b058-435d4d658064/B270i_2018_09_19_REACH_SVHC.PDF?tenant=ao-cert

List of Chemicals in Prop 65

STATE OF CALIFORNIA
ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT
SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986

CHEMICALS KNOWN TO THE STATE TO CAUSE CANCER OR REPRODUCTIVE TOXICITY
March 8, 2019

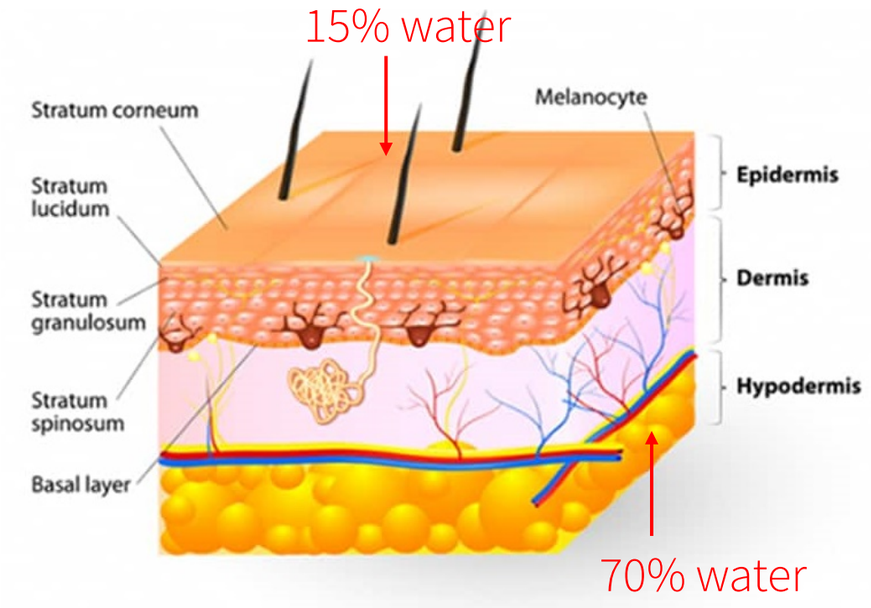
The Safe Drinking Water and Toxic Enforcement Act of 1986 requires that the Governor revise and republish at least once per year the list of chemicals known to the State to cause cancer or reproductive toxicity. The identification number indicated in the following list is the Chemical Abstracts Service (CAS) Registry Number. No CAS number is given when several substances are presented as a single listing. The date refers to the initial appearance of the chemical on the list. For easy reference, chemicals which are shown underlined are newly added. Chemicals or endpoints shown in strikeout were placed on the Proposition 65 list on the date noted, and have subsequently been removed.

Chemical	Type of Toxicity	CAS No.	Date Listed
A-alpha-C (2-Amino-9H-pyrido [2,3-b]indole)	Cancer	26148-68-5	January 1, 1990
Abiraterone acetate	developmental, female, male	154229-18-2	April 8, 2016
Acetaldehyde	Cancer	75-07-0	April 1, 1988
Acetamide	cancer	60-35-5	January 1, 1990
Acetazolamide	Developmental	59-66-5	August 20, 1999
Acetochlor	Cancer	34256-82-1	January 1, 1989
Acetohydroxamic acid	Developmental	546-88-3	April 1, 1990
2-Acetylaminofluorene	Cancer	53-96-3	July 1, 1987
Acifluorfen sodium	Cancer	62476-59-9	January 1, 1990
Acrylamide	Cancer	79-06-1	January 1, 1990
Acrylamide	developmental, male	79-06-1	February 25, 2011
Acrylonitrile	Cancer	107-13-1	July 1, 1987
Actinomycin D	Cancer Developmental	50-76-0	October 1, 1989 October 1, 1992
AF-2;[2-(2-furyl)-3-(5-nitro-2-furyl)] acrylamide	Cancer	3688-53-7	July 1, 1987
Aflatoxins	Cancer	—	January 1, 1988
Alachlor	Cancer	15972-60-8	January 1, 1989
Alcoholic beverages	Cancer	—	April 29, 2011
Alcoholic beverages, when associated with alcohol abuse	Cancer	—	July 1, 1988
Aldrin	cancer	309-00-2	July 1, 1988
All-trans retinoic acid	developmental	302-79-4	January 1, 1989
~~Allyl chloride~~ Delisted October 29, 1999	~~cancer~~	~~107-05-1~~	~~January 1, 1990~~
Aloe Vera, non-decolorized whole leaf extract	cancer	—	December 4, 2015
Alprazolam	developmental	28981-97-7	July 1, 1990
Altretamine	developmental, male	645-05-6	August 20, 1999
Amantadine hydrochloride	developmental	665-66-7	February 27, 2001
Amikacin sulfate	developmental	39831-55-5	July 1, 1990
2-Aminoanthraquinone	cancer	117-79-3	October 1, 1989
p-Aminoazobenzene	cancer	60-09-3	January 1, 1990
o-Aminoazotoluene	cancer	97-56-3	July 1, 1987

- Over 900 compounds in Prop 65 list
- Standard test method for Prop 65? Convert µg/g or µg/mL results into µg/day?
- OEHHA: “Proposition 65 does not specify what analytical test methods must be used to determine whether a discharge, release, or exposure contains a detectable amount of a chemical listed under the Act”

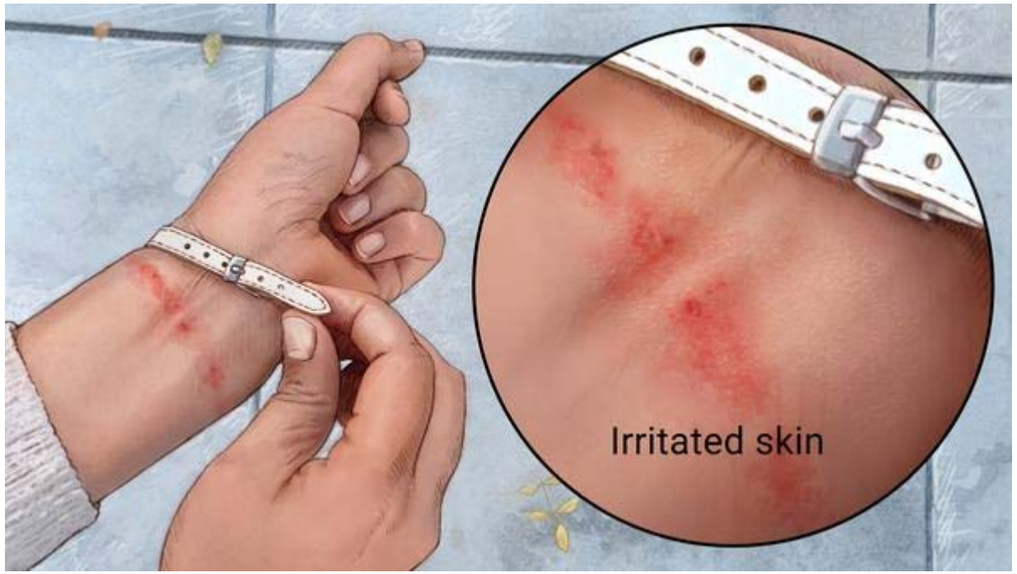
Dermal Health Effects

Dermal Effects Associated with Wearables



Moisture-Associated Skin Damage

Dermal Irritation

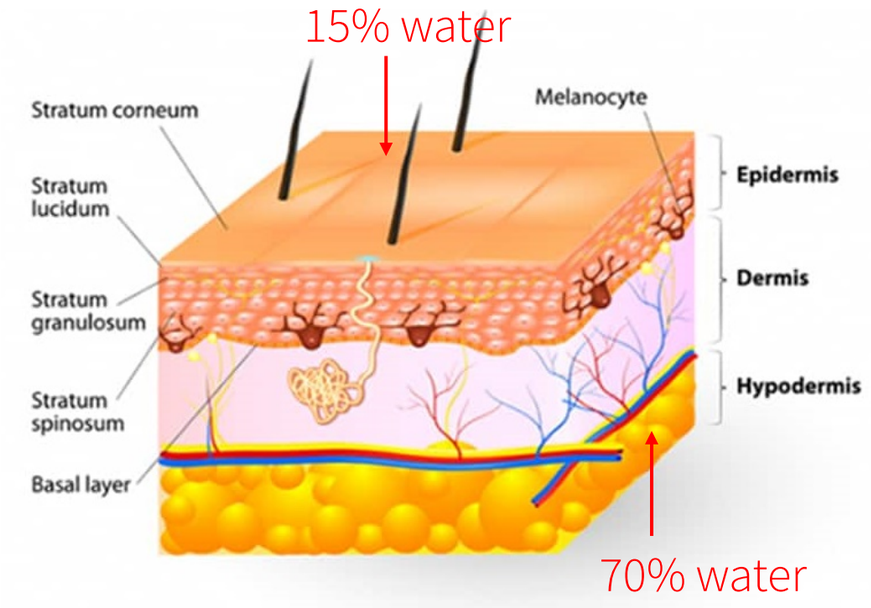


Allergic Contact Dermatitis

- Skin: complex and dynamic organ composed of an outer epidermis and inner dermis
- Has various functions, not just barrier to the external environment
- Dermal absorption is generally slow and less likely

https://www.bepanthen.co.uk/en/understanding-your-skin/your-skins-structure/
https://ntp.niehs.nih.gov/images/thumbnails/niceatm/ivdermal.jpg?1559543396244
https://www.mayoclinic.org/diseases-conditions/contact-dermatitis/symptoms-causes/syc-20352742
SE Anderson. Environ Health Insights. 2014; 8(Suppl 1): 51–62.

Moisture-Associated Skin Damage



Moisture-Associated Skin Damage

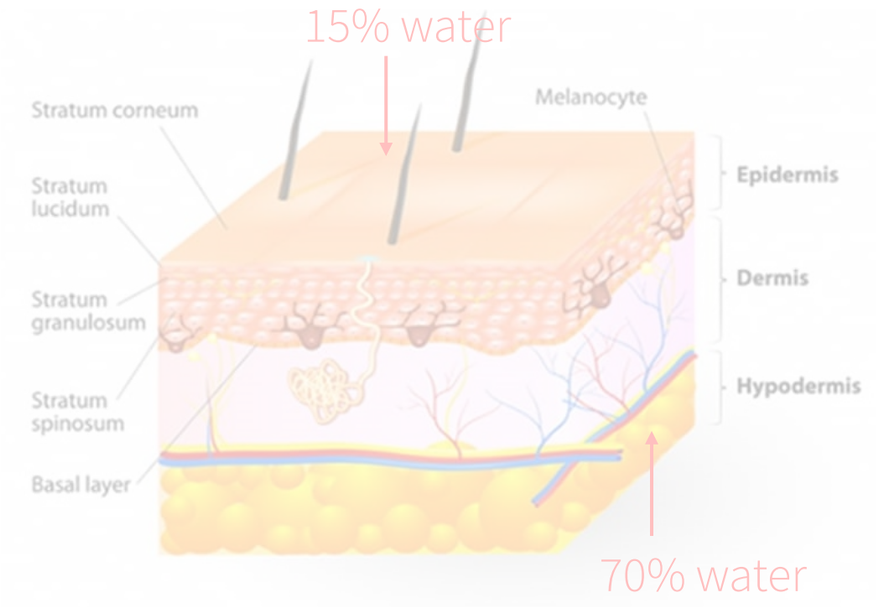
Dermal Irritation

Allergic Contact Dermatitis

- Moisture-associated skin damage from prolonged exposure to various sources of moisture and their contents
- Characterized by inflammation of the skin

M Gray. Moisture-associated skin damage: overview and pathophysiology. J Wound Ostomy Continence Nurs. 2011 May-Jun;38(3):233-41
https://www.bepanthen.co.uk/en/understanding-your-skin/your-skins-structure/
https://ntp.niehs.nih.gov/images/thumbnails/niceatm/ivdermal.jpg?1559543396244
https://www.mayoclinic.org/diseases-conditions/contact-dermatitis/symptoms-causes/syc-20352742

Dermal Irritation



Moisture-Associated Skin Damage

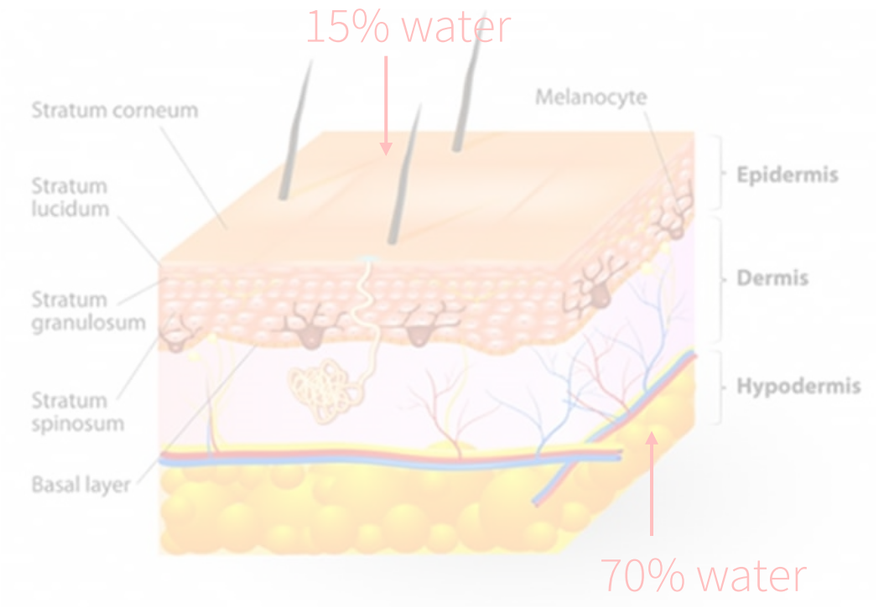
Dermal Irritation

Allergic Contact Dermatitis

- Non-immunological reaction
- Localized inflammation of the skin caused by direct damage following exposure
- Examples include certain organic solvent, sodium hydroxide

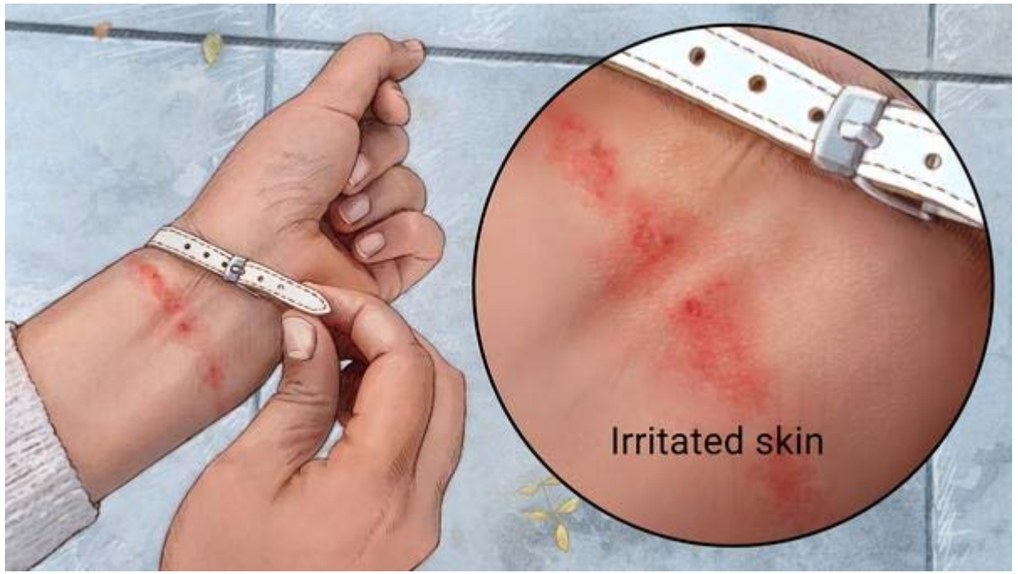
https://www.bepanthen.co.uk/en/understanding-your-skin/your-skins-structure/
https://ntp.niehs.nih.gov/images/thumbnails/niceatm/ivdermal.jpg?1559543396244
https://www.mayoclinic.org/diseases-conditions/contact-dermatitis/symptoms-causes/syc-20352742

Allergic Contact Dermatitis



Moisture-Associated Skin Damage

Dermal Irritation



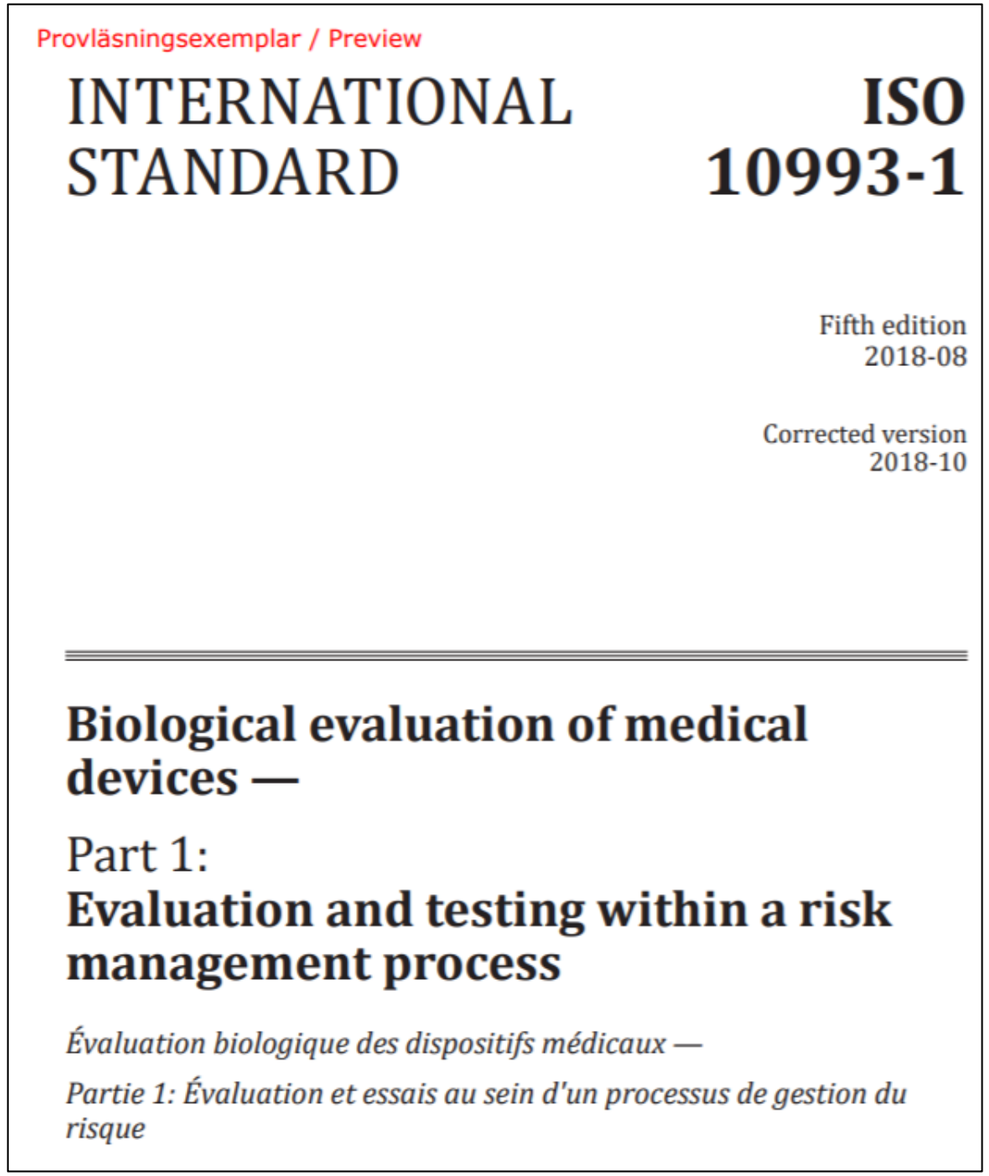
Allergic Contact Dermatitis

- Inflammation of the skin caused by an immunologic delayed hypersensitivity
- Reaction triggered by dermal contact to a skin allergen
- Repeated or chronic exposure to chemical sensitizer
- Examples include nickel, certain acrylates and methacrylates used in adhesive

https://www.bepanthen.co.uk/en/understanding-your-skin/your-skins-structure/
https://ntp.niehs.nih.gov/images/thumbnails/niceatm/ivdermal.jpg?1559543396244
https://www.mayoclinic.org/diseases-conditions/contact-dermatitis/symptoms-causes/syc-20352742

Standards for Biocompatibility Evaluation

ISO 10993 Biocompatibility Evaluation



Provläsningsexemplar / Preview

INTERNATIONAL STANDARD

ISO 10993-1

Fifth edition
2018-08

Corrected version
2018-10

Biological evaluation of medical devices —

Part 1:
Evaluation and testing within a risk management process

Évaluation biologique des dispositifs médicaux —

Partie 1: Évaluation et essais au sein d'un processus de gestion du risque

- ISO 10993-1: “The primary aim of this part of ISO 10993 is the protection of humans from potential risks arising from the use of medical devices”
- Measurement of how compatible a device is with a biological system

ISO 10993 Test Matrix Endpoints

Table A.1: Biocompatibility Evaluation Endpoints

Medical device categorization by			Biological effect												
Nature of Body Contact Category	Contact	Contact Duration A – limited (≤24 h) B – prolonged (>24 h to 30 d) C – permanent (> 30 d)	Cytotoxicity	Sensitization	Irritation or Intracutaneous Reactivity	Acute Systemic Toxicity	Material-Mediated Pyrogenicity	Subacute/Subchronic Toxicity	Genotoxicity	Implantation	Hemocompatibility	Chronic Toxicity	Carcinogenicity	Reproductive/Developmental Toxicity#	Degradation@
Surface device	Intact skin	A	X	X	X										
		B	X	X	X										
		C	X	X	X										
	Mucosal membrane	A	X	X	X										
		B	X	X	X	O	O	O		O					
		C	X	X	X	O	O	X	X	O		O			
	Breached or compromised surface	A	X	X	X	O	O								
		B	X	X	X	O	O	O		O					
		C	X	X	X	O	O	X	X	O		O	O		
External communicating device	Blood path, indirect	A	X	X	X	X	O				X				
		B	X	X	X	X	O	O			X				
		C	X	X	O	X	O	X	X	O	X	O	O		

- Wearable technologies are categorized under:
  - Intact skin contact
  - Limited (≤24 h) or
  - Prolonged (>24 h-30 d) contact duration

- Endpoints to test include:
  - Cytotoxicity
  - Sensitization
  - Irritation or intracutaneous reactivity

ISO 10993-12 Extraction Methods

INTERNATIONAL STANDARD

ISO 10993-12

Third edition
2007-11-15

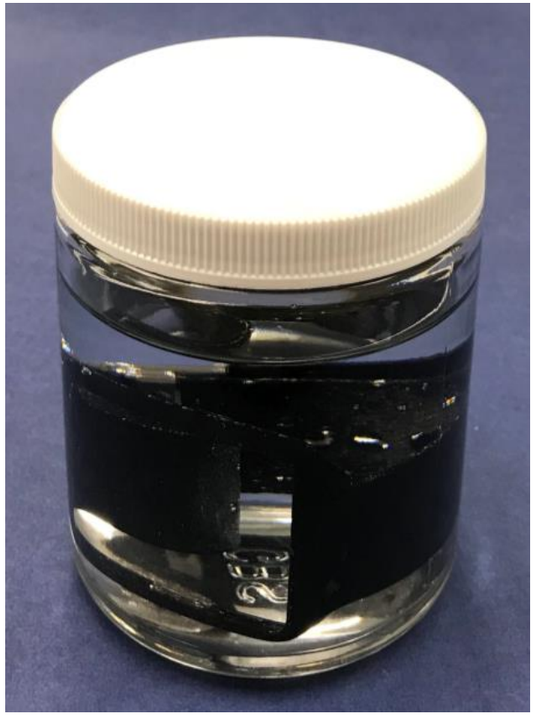
Corrected version
2008-02-15

Biological evaluation of medical devices —

Part 12:
Sample preparation and reference materials

Évaluation biologique des dispositifs médicaux —

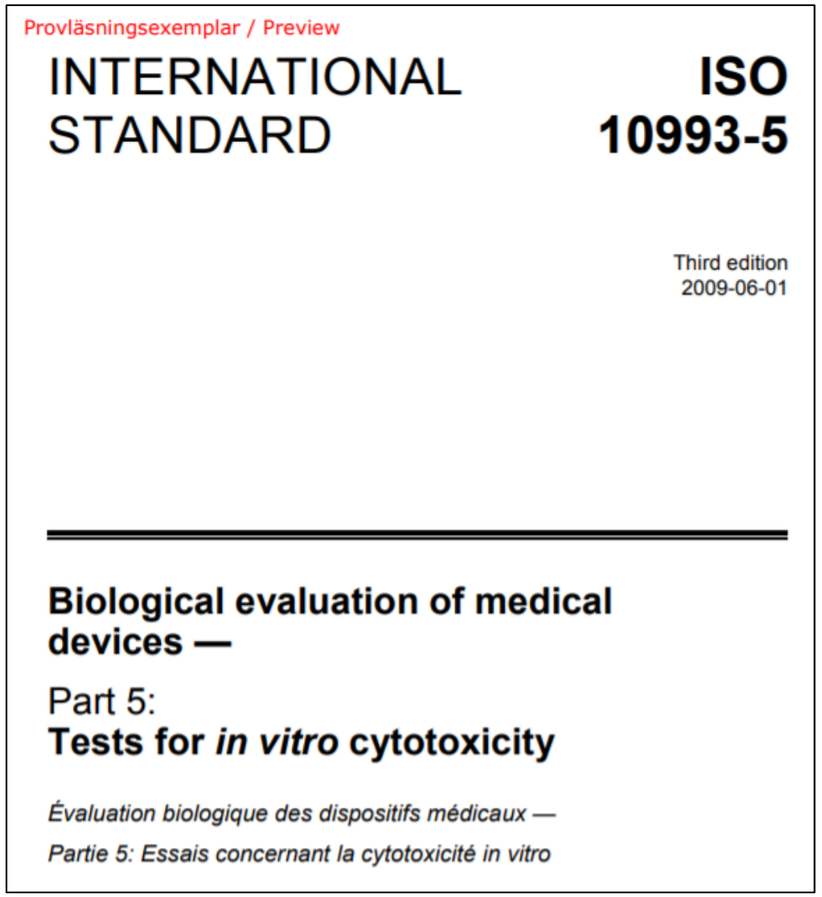
Partie 12: Préparation des échantillons et matériaux de référence

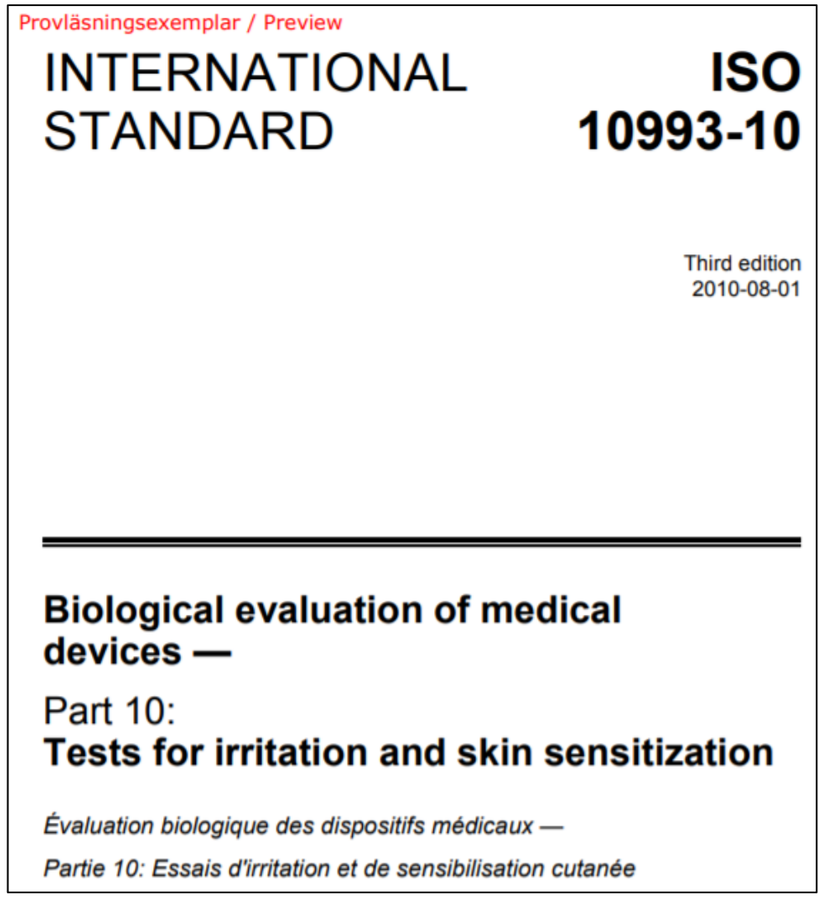


Extraction Analysis

- Extraction in polar and non-polar solvent
- Simulated use extraction in artificial sweat, saline, water
  - 37 °C for 72 hours
  - 50 °C for 72 hours
  - 70 °C for 24 hours
  - 121 °C for 1 hour
- Exaggerated extraction in organic solvent for hazard identification
  - Ensure that the exaggerated extraction does not result in a chemical change of the material

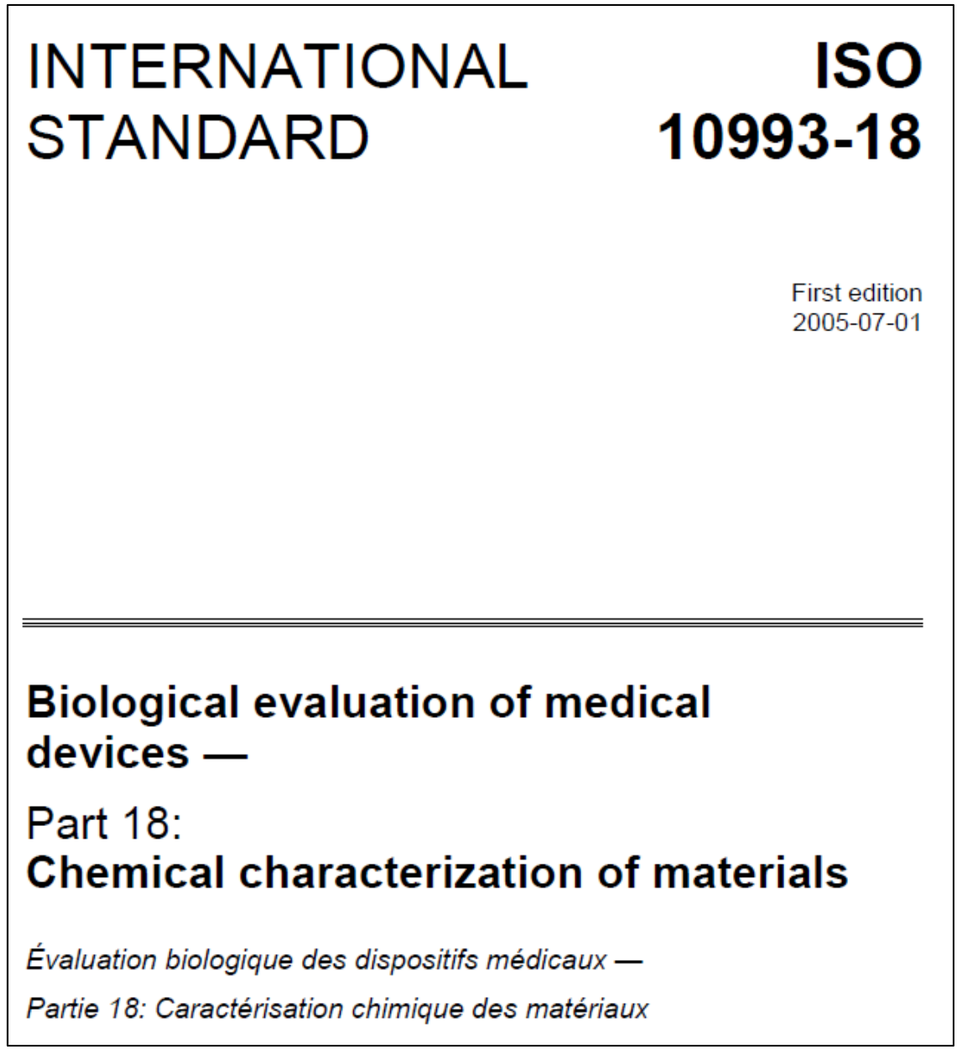
ISO 10993-5 and -10 Cytotoxicity & Irritation/Sensitization





- ISO 10993-5: use extracts on cell culture for cytotoxicity testing
- ISO 10993-10: use extracts/piece on rabbit for irritation and guinea pig for skin sensitization testing
- Cost and timing may be prohibitive

ISO 10993-18 Chemical Characterization


INTERNATIONAL STANDARD

ISO 10993-18

First edition
2005-07-01

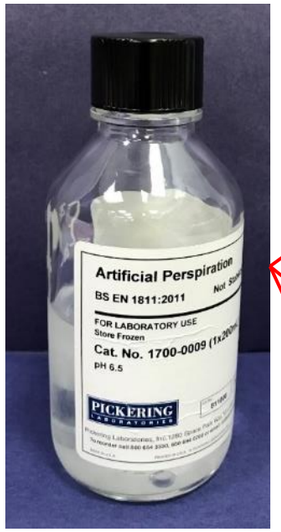
Biological evaluation of medical devices —

Part 18:
Chemical characterization of materials

Évaluation biologique des dispositifs médicaux —
Partie 18: Caractérisation chimique des matériaux

- Chemical characterization of extracts
- Gas chromatography – mass spectrometry (GC-MS) for analysis of volatile and semi-volatile organic compounds (VOCs and SVOCs)
- Liquid chromatography – mass spectrometry (LC-MS) for analysis of non-volatile organic compounds
- Inductively coupled plasma – mass spectrometry (ICP-MS) for analysis of metals

Simulated Product Handling



- Use of contact wipe can be a more accurate representation of user exposure scenarios compared to leach testing
- Testing complements leach testing
- Can be used to determine the potential exposures from standard use of the products (e.g. Prop 65)

GC-MS: Gas Chromatography Mass Spectrometry

Thermo Scientific 1310 GC with Single Quadrupole MS

Analysis of Environmental Stress Cracking on Plastic Surface

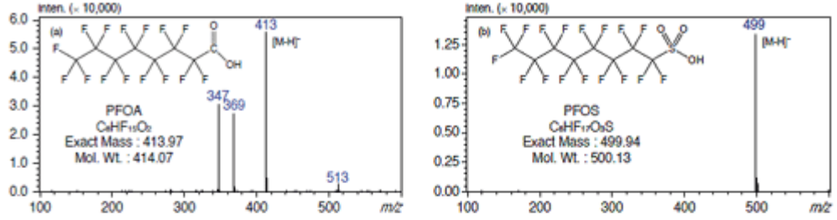
Example of Devices with Prolonged Dermal Contact

- Application: detecting volatile/semi-volatile, non-polar, and low molecular weight compounds (e.g. plasticizer, flame retardant, polymeric monomer and additive)
- Example 1: analysis of environmental stress cracking in plastic material from compounds in topical or household products (e.g. sunscreen, insect repellants, cleaning solutions)
- Example 2: analysis of leachable organic compounds from wearable devices

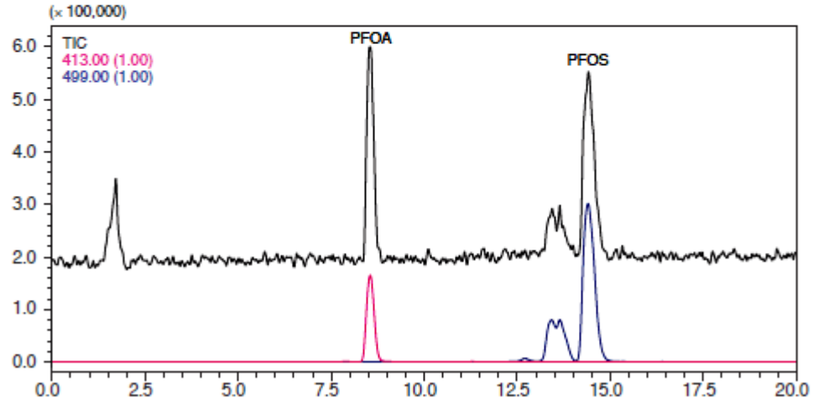
http://www.plastics.gl/resources/image/articles/2013/issue7+8/UGP_Eastman_UseIt/eastman_bu2_chemical_resistance_plaques_web.jpg
http://i.dailymail.co.uk/i/pix/2016/09/21/16/38A72B8400000578-3800396-image-a-46_1474472741875.jpg

LC-MS: Liquid Chromatography Mass Spectrometry

Waters Acquity UPLC- Xevo XS QTOF-MS



ESI Mass Spectra of PFOA and PFOS



Total Ion Chromatogram and Mass Chromatogram of PFOA and PFOS (each 1 mg/L)

Analysis of Organofluorine Compounds

- Application: Detecting non-volatile, polar, and larger compounds (e.g. dyes, polymer additives)
- Example: detecting organofluorine compounds (e.g. perfluorooctanoic acid (PFOA) or perfluorooctanesulfonic acid (PFOS)) from wearable devices

https://www.shimadzu.com/an/industry/environment/e8o1ci0000000a32.htm

ICP-MS: Inductively Coupled Plasma Mass Spectrometry

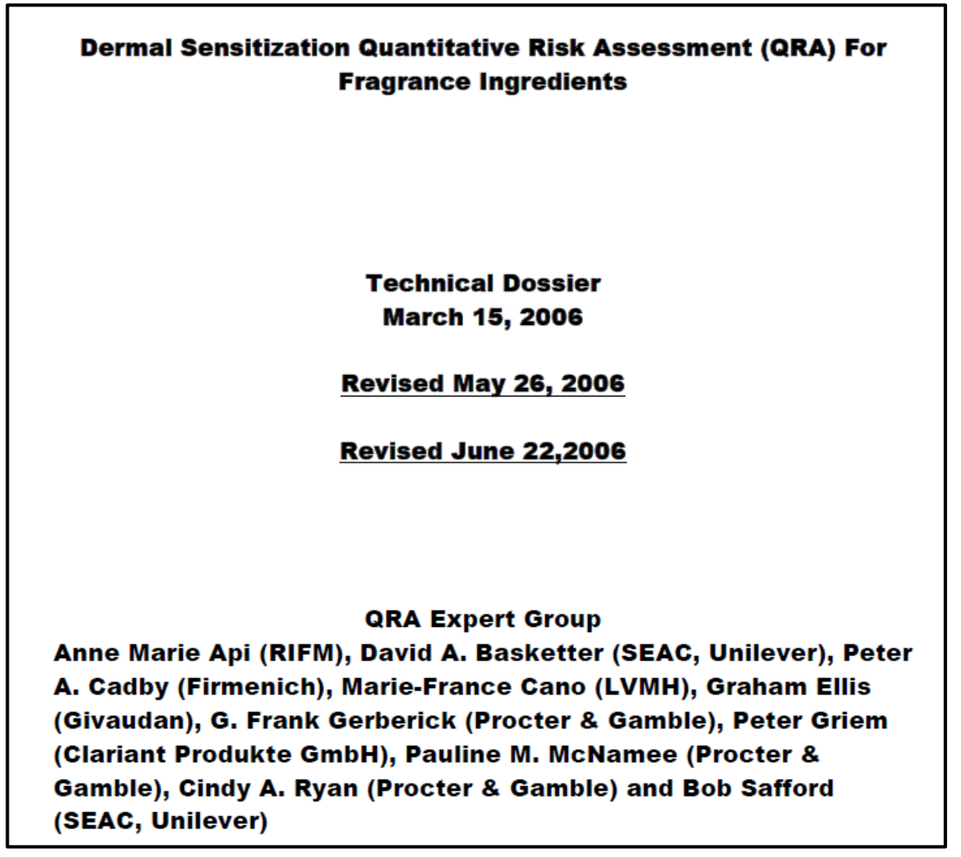
PerkinElmer NexION 2000 B

BS EN 1811 Nickel Release

- Application: detecting metals (e.g. nickel, cobalt, chromium, lead, or others) in the extracts
- Example 1: Prop 65 analysis for lead content
- Example 2: detecting nickel content

https://www.perkinelmer.com/lab-solutions/resources/images_for_resize/NexION_2000B_ICP-MS_Right_Elevated.png

Dermal QRA and ISO 10993-17 Risk Assessment



Dermal Sensitization Quantitative Risk Assessment (QRA) For Fragrance Ingredients

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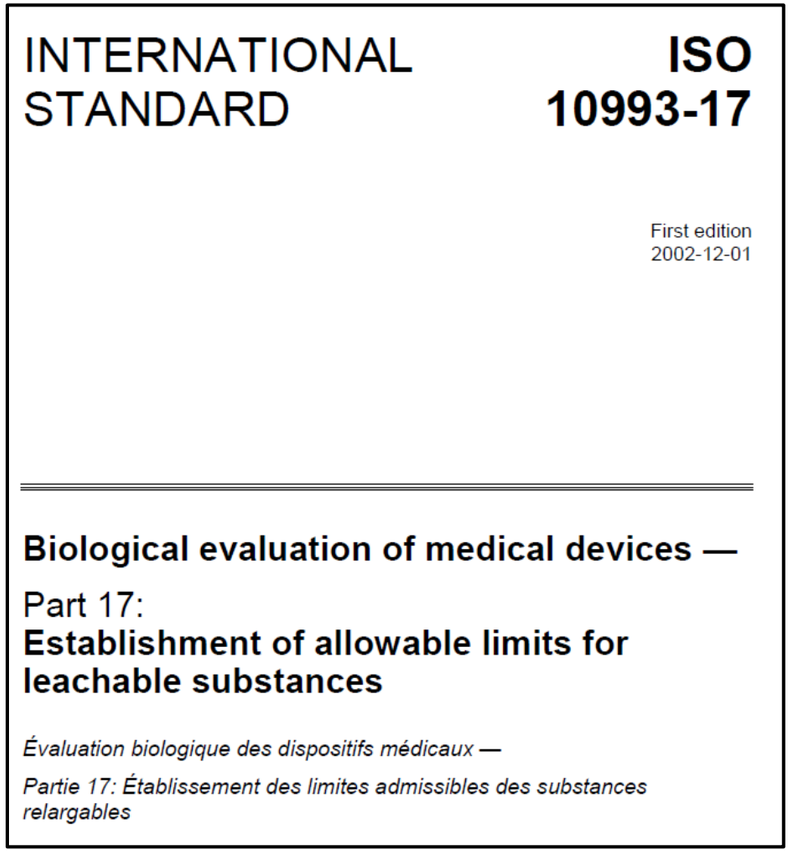
March 15, 2006

Revised May 26, 2006

Revised June 22,2006

QRA Expert Group
Anne Marie Api (RIFM), David A. Basketter (SEAC, Unilever), Peter A. Cadby (Firmenich), Marie-France Cano (LVMH), Graham Ellis (Givaudan), G. Frank Gerberick (Procter & Gamble), Peter Griem (Clariant Produkte GmbH), Pauline M. McNamee (Procter & Gamble), Cindy A. Ryan (Procter & Gamble) and Bob Safford (SEAC, Unilever)



INTERNATIONAL STANDARD **ISO 10993-17**

First edition
2002-12-01

Biological evaluation of medical devices —

Part 17:
Establishment of allowable limits for leachable substances

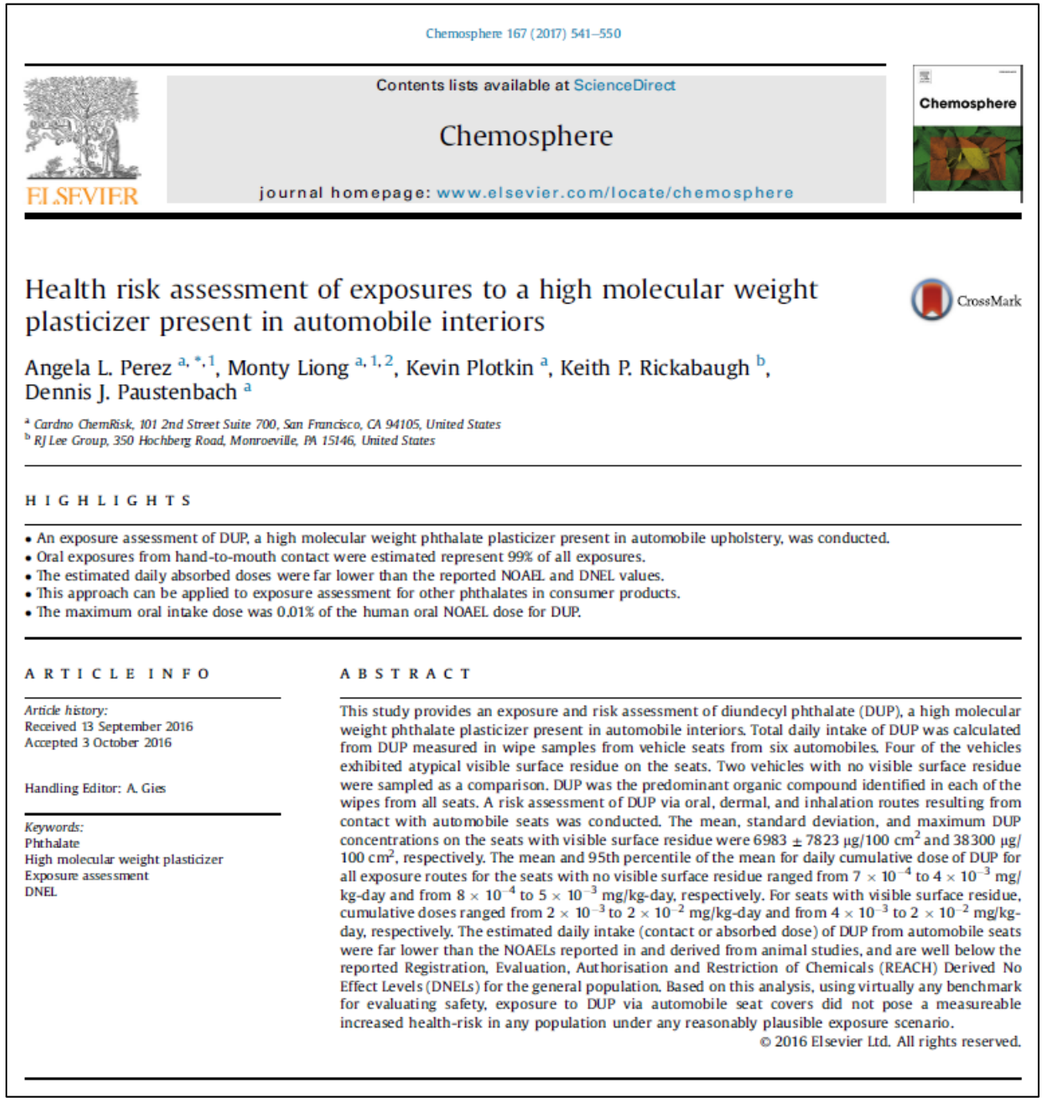
Évaluation biologique des dispositifs médicaux —

Partie 17: Établissement des limites admissibles des substances relargables

- Risk assessment methods to determine if the device can cause skin irritation or sensitization
- Review publicly available databases to check for known health effects of the compounds:
  - ECHA database: https://echa.europa.eu/
  - NCBI PubChem database: https://pubchem.ncbi.nlm.nih.gov/

Example Project 1 – Automobile Interior

Exposure Assessment for Automobile Interiors



Chemosphere 167 (2017) 541–550

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journal homepage: www.elsevier.com/locate/chemosphere

Health risk assessment of exposures to a high molecular weight plasticizer present in automobile interiors

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[b] RJ Lee Group, 350 Hochberg Road, Monroeville, PA 15146, United States

HIGHLIGHTS

- An exposure assessment of DUP, a high molecular weight phthalate plasticizer present in automobile upholstery, was conducted.
- Oral exposures from hand-to-mouth contact were estimated represent 99% of all exposures.
- The estimated daily absorbed doses were far lower than the reported NOAEL and DNEL values.
- This approach can be applied to exposure assessment for other phthalates in consumer products.
- The maximum oral intake dose was 0.01% of the human oral NOAEL dose for DUP.

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ABSTRACT

This study provides an exposure and risk assessment of diundecyl phthalate (DUP), a high molecular weight phthalate plasticizer present in automobile interiors. Total daily intake of DUP was calculated from DUP measured in wipe samples from vehicle seats from six automobiles. Four of the vehicles exhibited atypical visible surface residue on the seats. Two vehicles with no visible surface residue were sampled as a comparison. DUP was the predominant organic compound identified in each of the wipes from all seats. A risk assessment of DUP via oral, dermal, and inhalation routes resulting from contact with automobile seats was conducted. The mean, standard deviation, and maximum DUP concentrations on the seats with visible surface residue were 6983 ± 7823 μg/100 cm^2 and 38300 μg/100 cm^2, respectively. The mean and 95th percentile of the mean for daily cumulative dose of DUP for all exposure routes for the seats with no visible surface residue ranged from 7×10^{-4} to 4×10^{-3} mg/kg-day and from 8×10^{-4} to 5×10^{-3} mg/kg-day, respectively. For seats with visible surface residue, cumulative doses ranged from 2×10^{-3} to 2×10^{-2} mg/kg-day and from 4×10^{-3} to 2×10^{-2} mg/kg-day, respectively. The estimated daily intake (contact or absorbed dose) of DUP from automobile seats were far lower than the NOAELs reported in and derived from animal studies, and are well below the reported Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Derived No Effect Levels (DNELs) for the general population. Based on this analysis, using virtually any benchmark for evaluating safety, exposure to DUP via automobile seat covers did not pose a measureable increased health-risk in any population under any reasonably plausible exposure scenario.

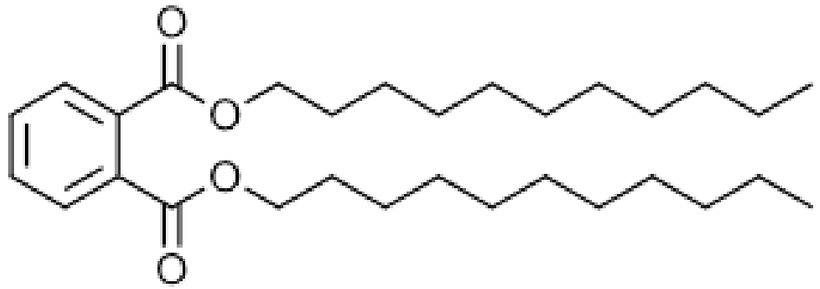
- Identification and quantification of chemical(s) of interest present in the product
- Quantitative evaluation of the different pathways where consumers are potentially exposed to the chemical(s) of interest from standard use of the product
- Determination of the potential human health risk from these exposures

Residues on Car Seat

- Residues were observed on artificial leather (polyvinyl chloride-based) seats in automobile interiors
- Wipe sampling was performed to ID the residue and determine the estimated concentration per surface area
- Extract from wipe sample was analyzed using gas chromatography-mass spectrometry (GC-MS)

https://ae01.alicdn.com/kf/HTB1fCExHVXXXXcmXpXXq6xXFXXXE/Synthetic-Leather-Car-Seat-Covers-10pcs-for-5-seats-Black-universal-covers.jpg_640x640.jpg

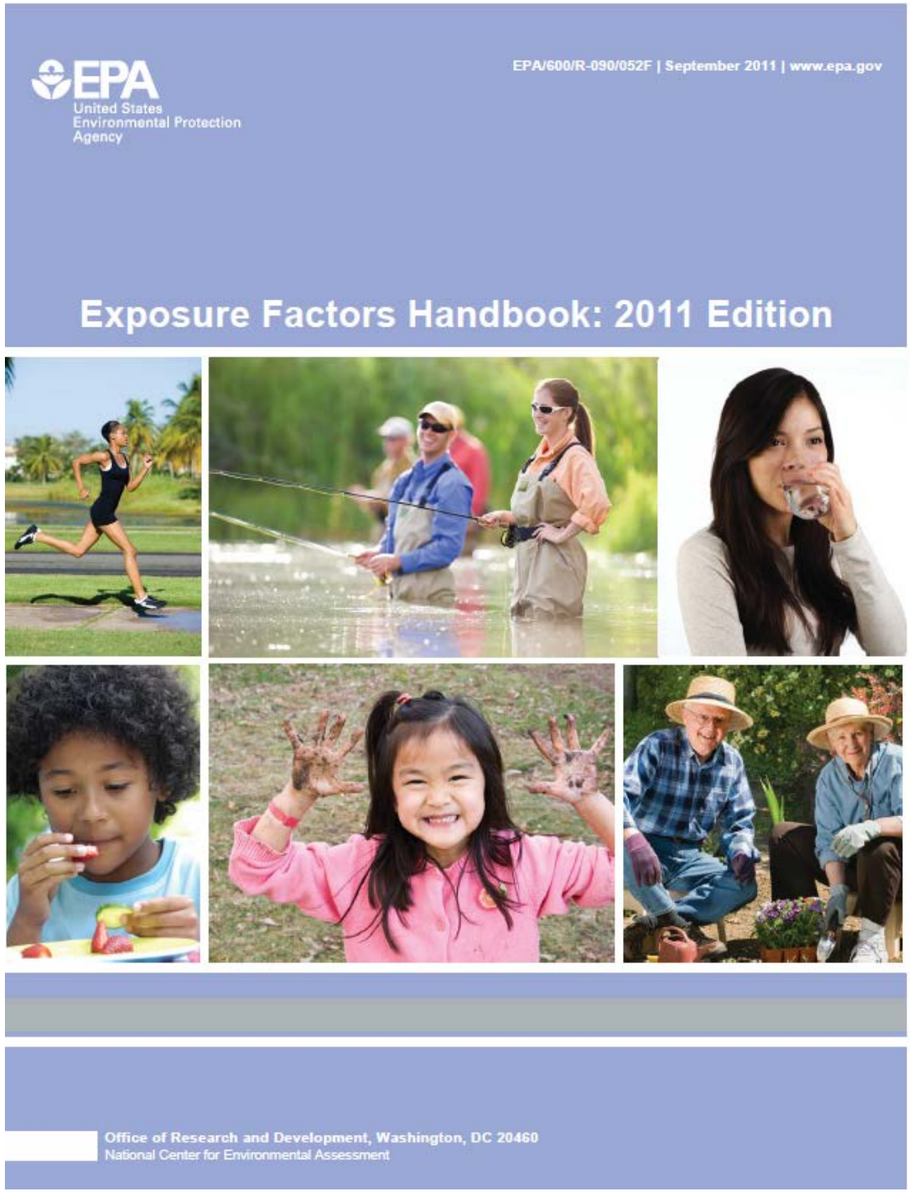
Identification of Residue



Molecular structure of diundecyl phthalate (DUP)

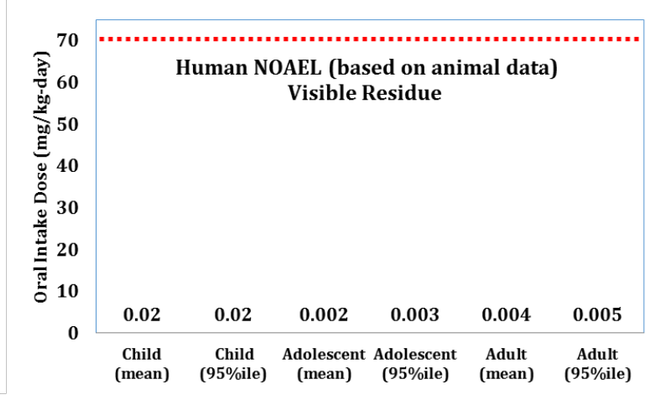
- Diundecyl phthalate (DUP, CAS# 3648-20-2) was the organic compound identified in each of the wipe samples
- High molecular weight phthalate plasticizers such as DUP are commonly used in components of automobile interiors
- Phthalate plasticizers are not covalently bound to the polymeric materials

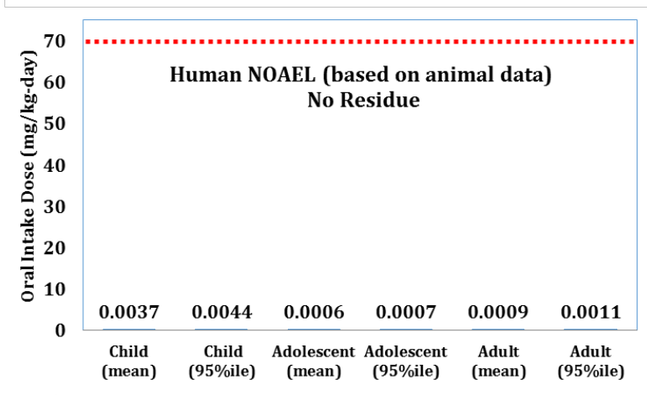
Evaluate Exposure Pathways for Residue

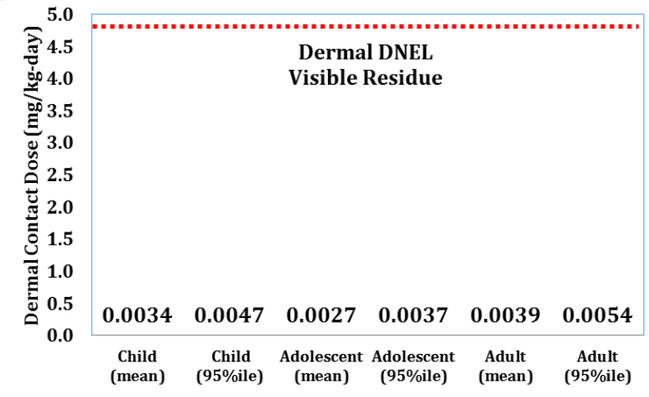


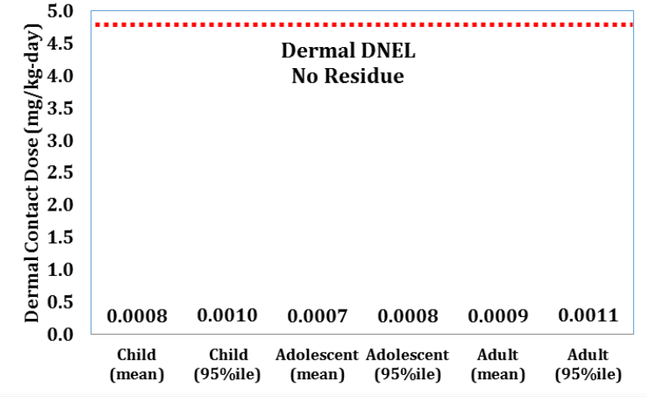
- Oral, dermal, and inhalation exposures
- EPA Exposure Factors Handbook as guidelines
- Surface areas, body weight
- Transfer factor from seat to skin, and from skin to mouth

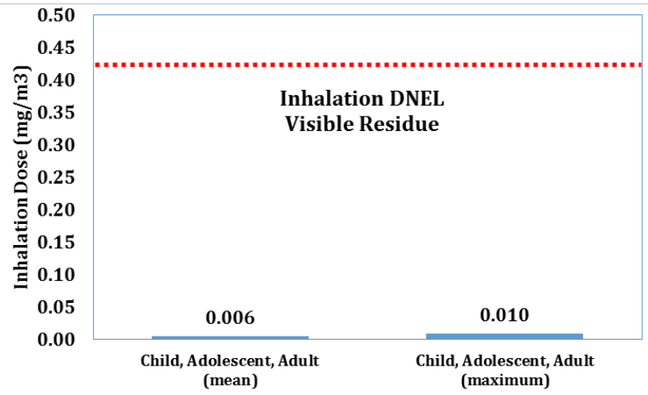
Risk Assessment of Exposure to Residue

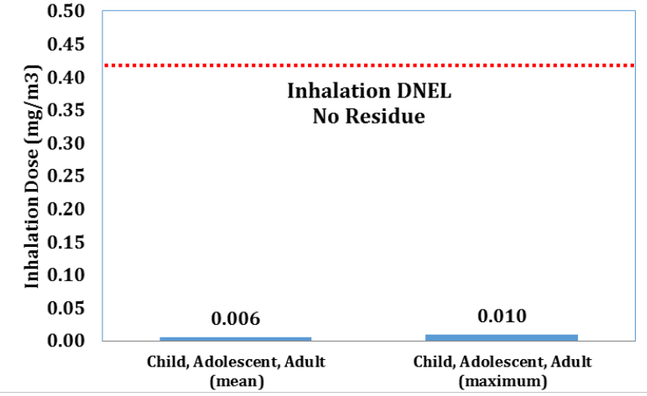












- Estimated daily doses for DUP from automobile seats were compared with:
  - Derived reference doses based on animal studies
  - Derived no-effect levels (DNELs) listed by the European Chemicals Agency (ECHA)
- The estimated daily absorbed doses were lower than the reference doses and DNEL values

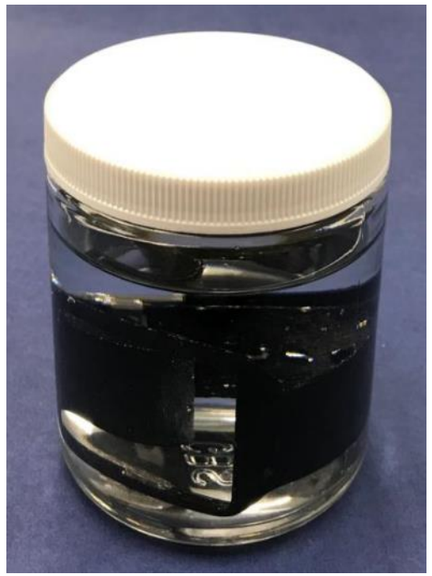
Example Project 2 – Wearable

Claim of Skin Irritation/Sensitization

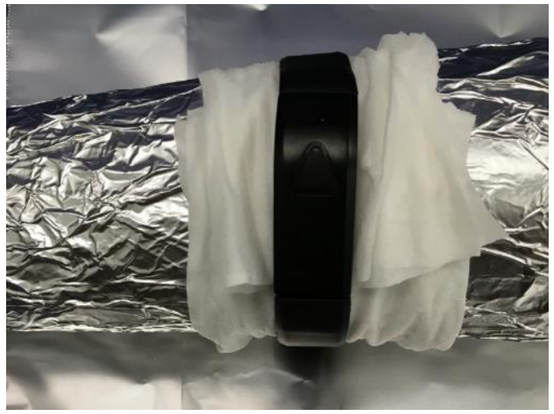
- Claims of skin irritation or sensitization from wearing devices
- Devices remain functional
- No signs of thermal damage

https://contestimg.wish.com/api/webimage/5b99fda80fc3e348d8f3a466-large.jpg?cache_buster=3d9e04d7cb81c596c621be602e8142e8

Identification of Chemicals in Extracts



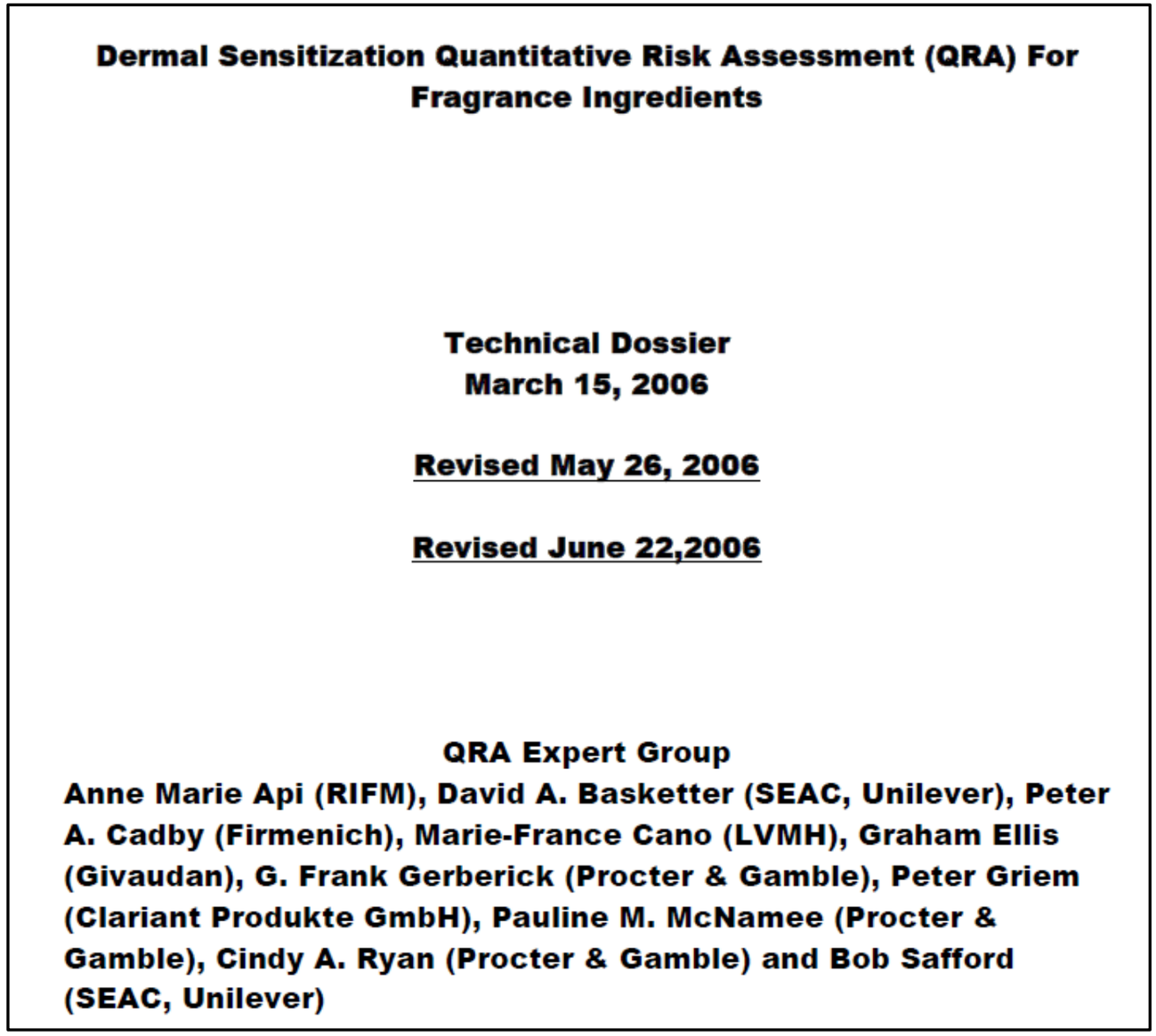
Leach Testing



Simulated Product Handling

- Leach testing in artificial sweat and organic solvent
- Simulated product handling using contact wipe and artificial sweat
- Analysis for organic compounds and metals in the solution extracts and wipe extracts
- Identified nickel in the extracts

Dermal QRA Method



Dermal Sensitization Quantitative Risk Assessment (QRA) For Fragrance Ingredients

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- Dermal quantitative risk assessment (QRA) for skin sensitization or irritation on compounds in extracts:

1. Determine a toxicity reference value, no-effect, or minimum effect level for skin sensitization

2. Determine estimated applied dose

3. Calculate hazard quotient (HQ)
   a) HQ = estimated applied dose/DNEL (Derived No Effect Level), MET (Minimum Elicitation Concentration), or AEL (Acceptable Exposure Level)
   b) If HQ > 1, this indicates that there may be potential for skin sensitization
   c) If HQ < 1, this indicates that use of the device likely does not pose skin irritation or sensitization related to these compounds

Dermal Quantitative Risk Assessment (QRA)

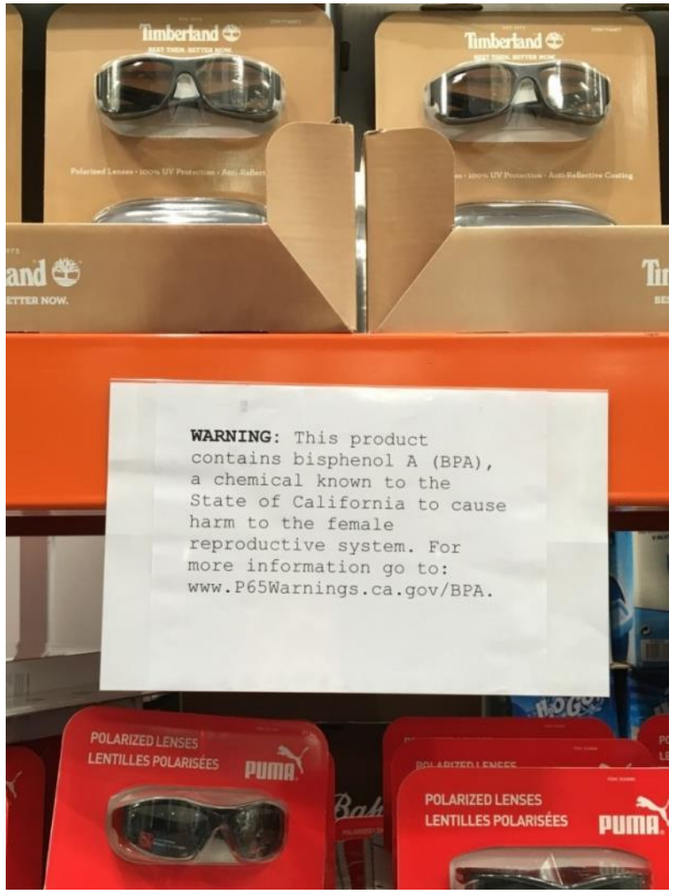
Local effects	
Long term exposure	
Hazard assessment conclusion:	DNEL (Derived No Effect Level)
Value:	0.035 mg/cm²
Most sensitive endpoint:	sensitisation (skin)
DNEL related information	
Overall assessment factor (AF):	2
Dose descriptor:	other: NOAEL
Acute/short term exposure	
Hazard assessment conclusion:	no hazard identified

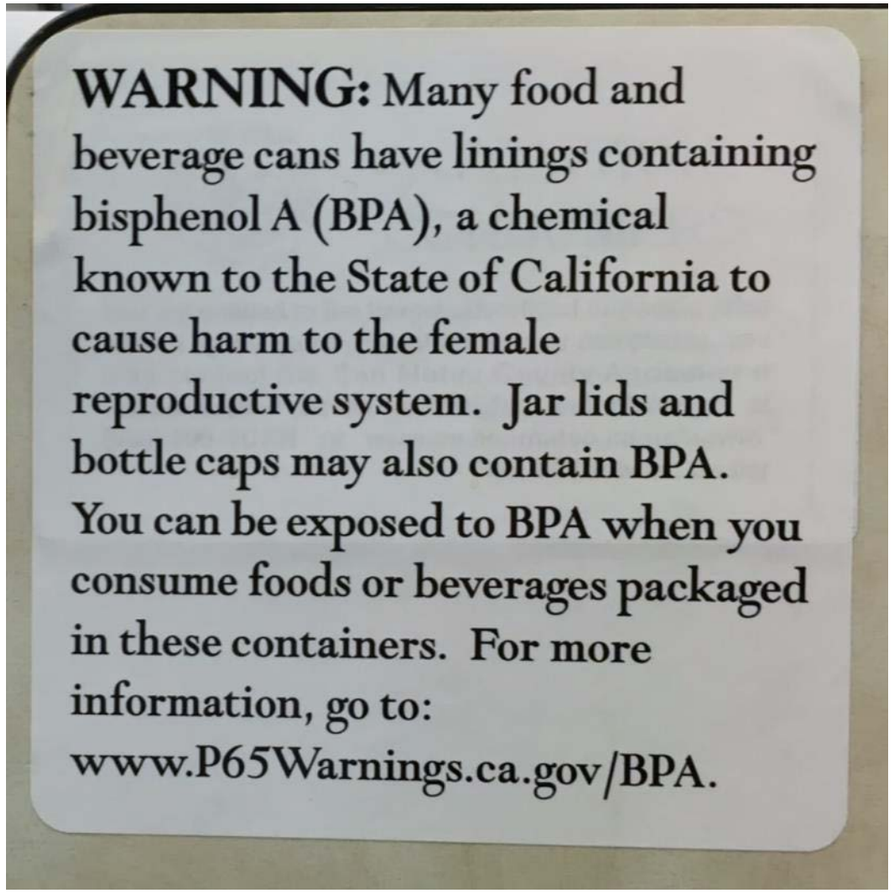
ECHA Registration Dossier for Nickel

- Compare with ECHA Registration Dossier for nickel
- Estimated applied doses of nickel from extraction and simulated product handling are less than the Derived No Effect Level
- HQ < 1: skin sensitization not expected

Example 3 – Bisphenol A in Prop 65

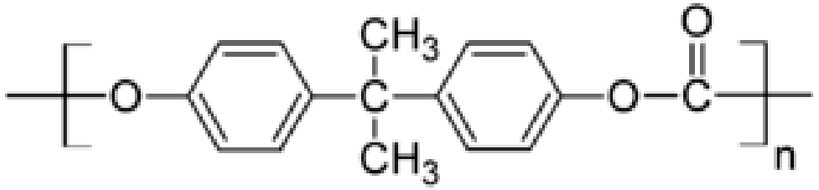
Prop 65 Regulation for Bisphenol A (BPA)



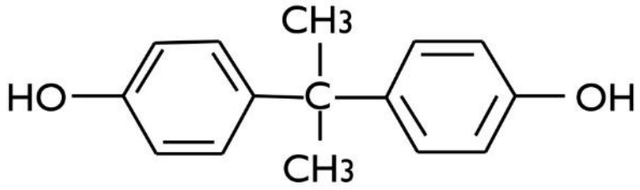


- Maximum Allowable Dose Level (MADL) of 3 µg/day for BPA from dermal exposure of solid materials

BPA in Polycarbonate-Containing Products



Polycarbonate



BPA

- BPA is used in the production of polycarbonate-based materials
  - Release of BPA can occur from degradation of polycarbonate-based materials
- Factors that can accelerate degradation of polycarbonate include:
  - Moisture
  - High temperature
  - Presence of amine/basic species (may be used as additives or in packaging materials)
  - UV light

Examples of Polycarbonate-Based Products

- Examples of polycarbonate-containing products include:
  - Power adapters, fitness trackers, routers, eyeglasses, medical devices
- Convert leach test results (in µg BPA/L or µg BPA/g) into µg BPA/day requires assumptions
- Use simulated product handling to get µg BPA/day

Simulated Product Handling

- Simulated product handling to determine the daily level of exposure as indicated in California Code of Regulations 27 CCR § 25821

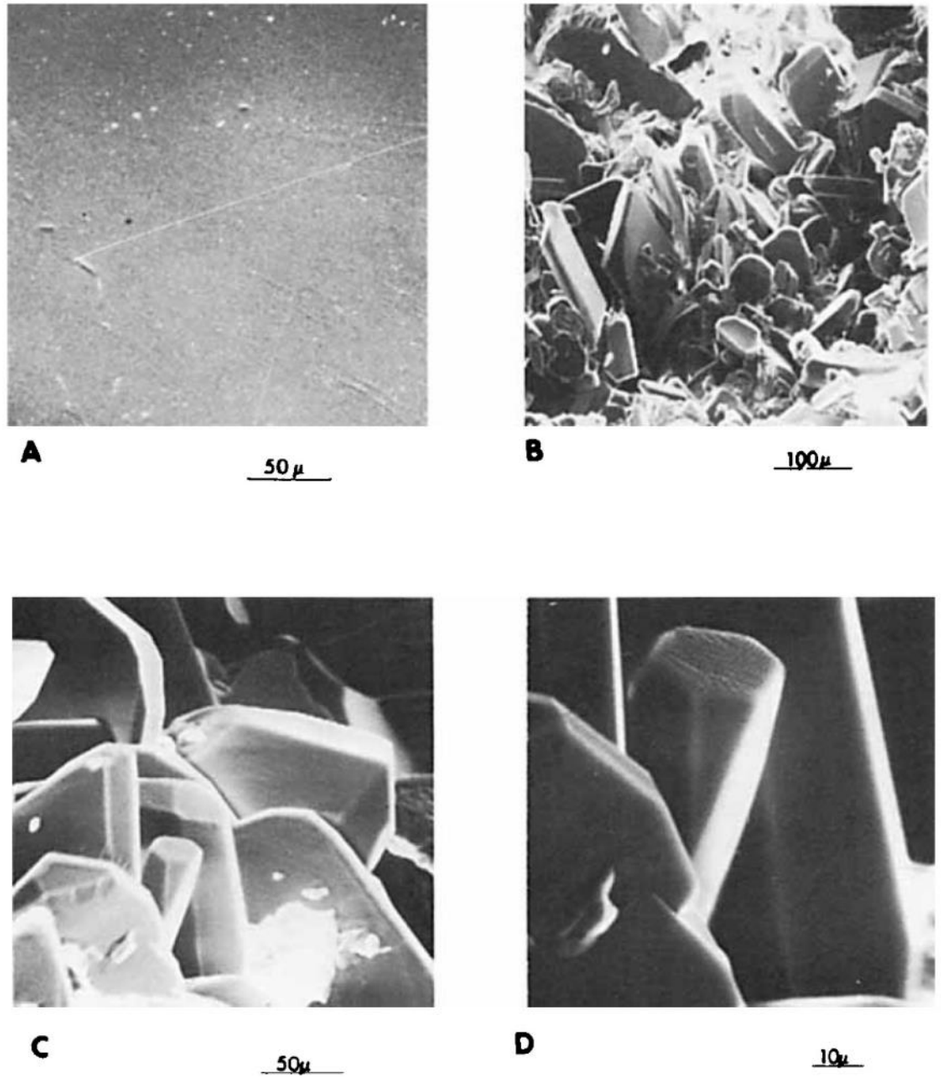
- CCR § 25821 specifies that “for exposures to consumer products, the level of exposure shall be calculated using the reasonably anticipated rate of intake or exposure for average users of the consumer product, and not on a per capita basis for the general population”

- The total amounts of BPA detected in the wipe samples (in µg/wipe) from simulated product handling were estimated as a daily level of exposure (in µg/day)

Simulated Product Handling

- Simulated product handling is based on wipe sampling protocols described in NIOSH 9100 and ASTM D6661
- Ghost Wipes, recommended by OSHA for surface sampling of organic compounds and metals, can be used as the contact wipes
- BS EN 1811 artificial sweat can be used as the solvent for contact wipes

Release of BPA from Polycarbonate



- Elevated temperature, humidity, alkaline species can influence the hydrolysis of polycarbonate, which would lead to the release of BPA
- Images show formation of BPA on:
  A. Polycarbonate surface aged 102 days at 85 °C
  B. Polycarbonate surface aged 102 days at 85 °C and 96% relative humidity
  C. Polycarbonate surface aged 102 days at 85 °C and 96% relative humidity (higher magnification)
  D. Polycarbonate surface aged 102 days at 85 °C and 96% relative humidity (higher magnification)

Bair H.E., et al. Hydrolysis of Polycarbonate to Yield BPA. J. Appl. Polymer. Sci., 1981, 26: 1777.

Accelerated Aging Tests

$$t_E = t_T * Q_{10}^{(T-T_{RT})/10}$$

Where

t_E	Equivalent time at ambient temperature and 50% relative humidity
t_T	Accelerated-aging time
T	Accelerated-aging temperature, degrees Celsius
T_{RT}	Ambient temperature, 23°C
Q_{10}	Accelerated-aging factor

Desired Real Time (RT): 24 months

Accelerated Aging Temperature (T_{AA}): 55 °C

Notes: WESTPAK does not recommend aging packaging materials at temperatures exceeding +60°C. Common AATs are +50°C, +55°C and +60°C.

Ambient Temperature (T_{RT}): 25 °C

Notes: This temperature is typically between +20°C to +25°C. A temperature of +25°C is a more conservative approach.

Aging Factor (Q_{10}): 2

Note: This factor is typically between 1.8 to 2.5 with a value of 2.0 being the most common value.

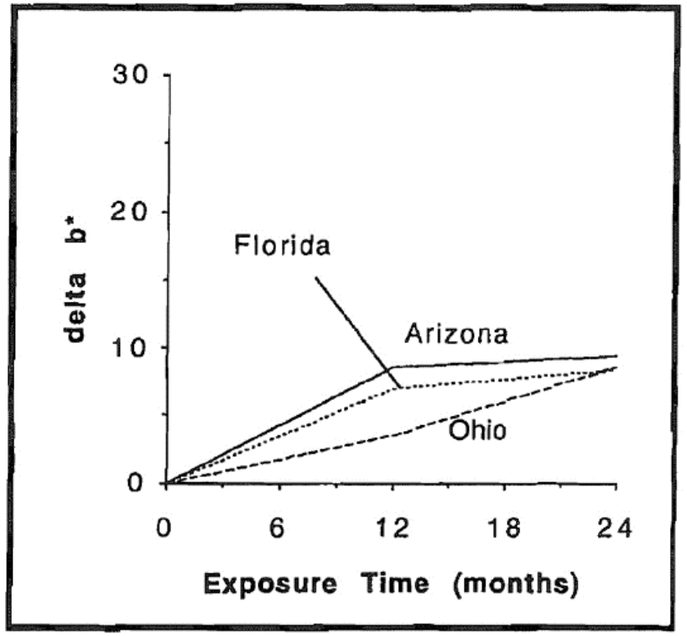
CLICK TO CALCULATE ACCELERATED TIME

Calculated Accelerated Aging Time (AAT): 91.3 days

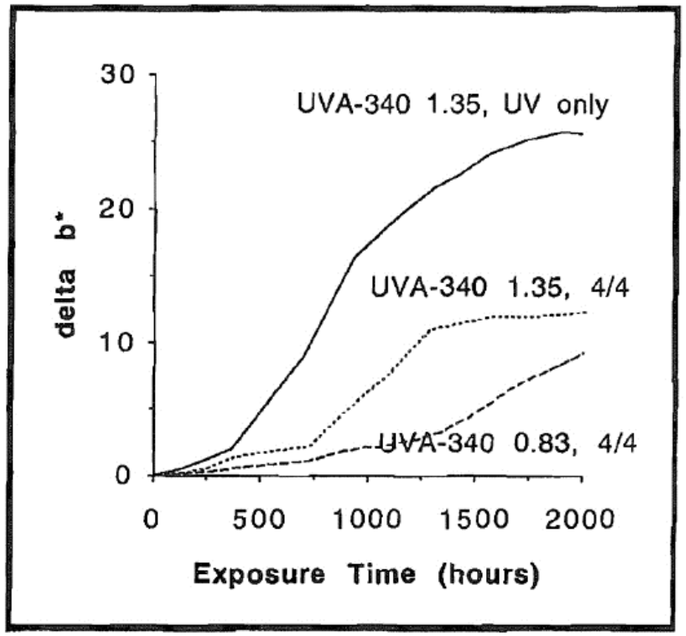
- Accelerated aging tests using ASTM F1980 as a guide
  - ASTM F1980 – Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices
- Investigate how the release of BPA from the product can change over a period of time

https://www.westpak.com/page/resources/accelerated-aging-time-calculator

QUV Accelerated Weathering Tests



Change in color/gloss of polycarbonate from outdoor exposure

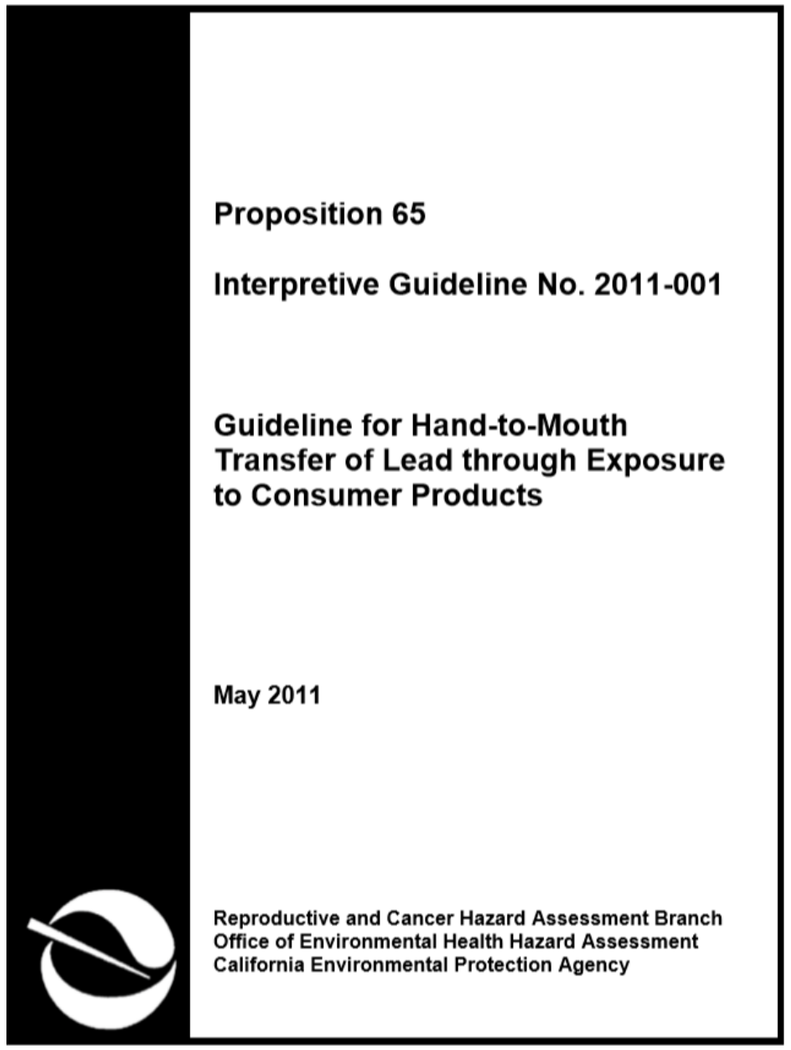


Change in color/gloss of polycarbonate from QUV exposure

- QUV accelerated weathering tests using ASTM G154 as a guide
  - ASTM G154: Standard Practice for Operating Fluorescent Ultraviolet (UV) Lamp Apparatus for Exposure of Nonmetallic Materials
- Investigate how the release of BPA from the product can change from exposure of direct sunlight

Hareesh K., et al. Changes in the properties of Lexan polycarbonate by UV irradiation. Nucl. Instr. Meth. B, 2013, 295: 61.
Fedor, G. R., and Brennan, P. J., "Comparison Between Natural Wathering and Fluorescent UV Exposures: UVA-340 Lamp Test Results," Durability Testing of Non-Metallic Materials, ASTM STP 1294, Robert J. Herling, Ed., American Society for Testing and Material, Philadelphia, 1996.

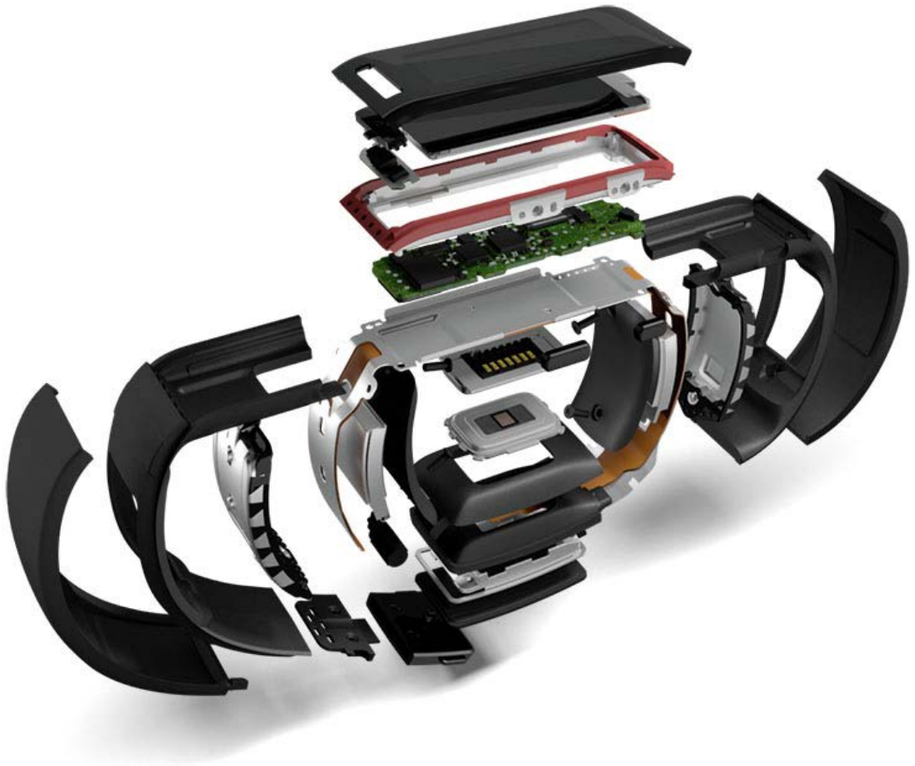
Transfer Factor



- Similar analysis can be performed for other compounds in Prop 65
- For lead and lead compounds, Prop 65 Maximum Allowable Dose Level (MADL) of 0.5 µg/day
- The hand-to-mouth transfer factor will further reduce the exposure to lead
- According to OEHHA, the direct hand-to-mouth transfer factor of 50% is selected as the default value for lead in consumer products

Example 4 – Release of New Products

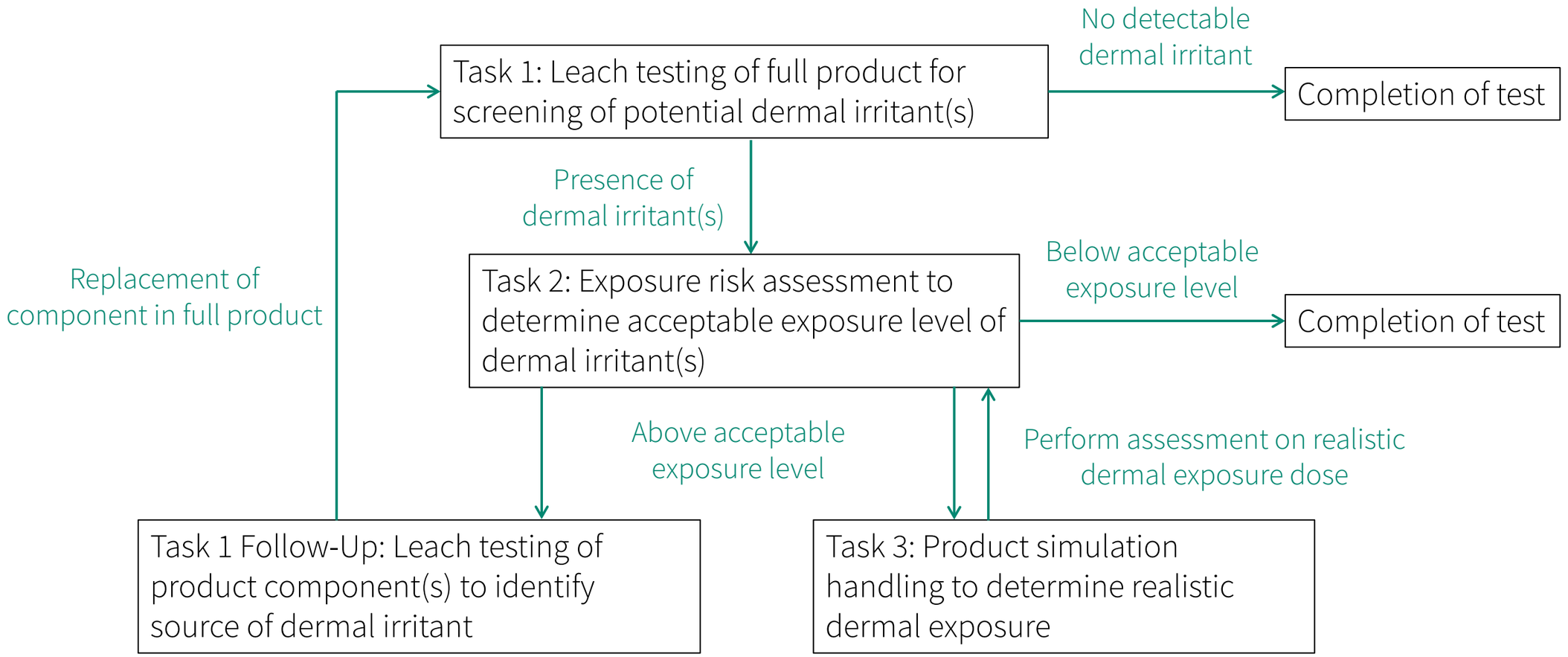
Release of New Products: Procedures



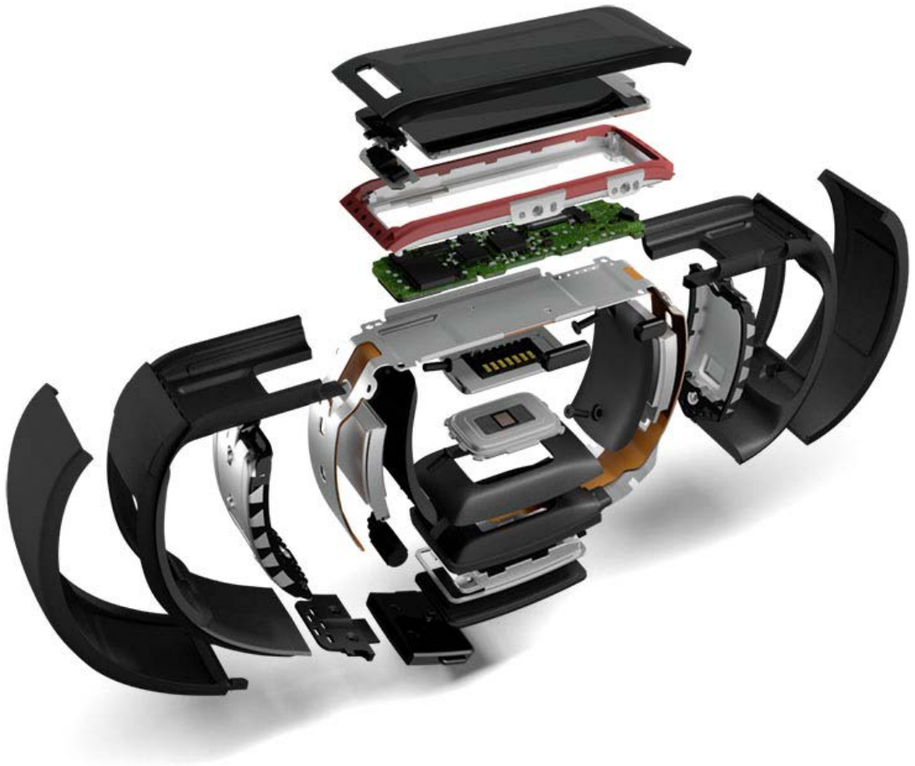
- Review bill of materials (BOM) to identify components that are likely to be in contact with the skin
- Review safety data sheets (SDS) and available test reports for these components
  - EN 1811, RoHS, REACH SVHC
- Leach testing of assembled products (without interior electronic components)
- Contact wipe testing or simulated product handling

Arstechnica.com

Flow Chart for Biocompatibility Analysis



Release of New Products: Procedures



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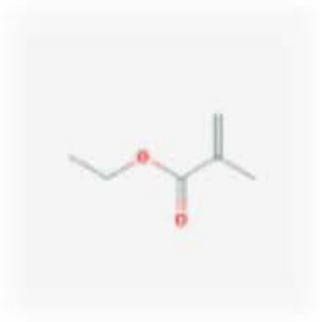
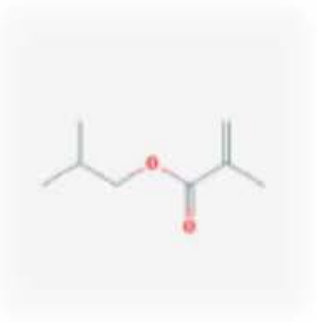
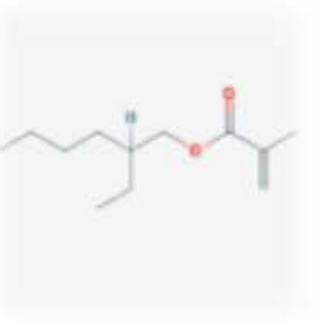
Arstechnica.com

Unknown Acceptable Exposure Levels

Methyl Methacrylate	Ethyl Methacrylate	i-Butyl Methacrylate	n-Butyl Methacrylate	2-Ethylhexyl Methacrylate
				

- Some compounds do not have sufficient toxicity data
- Use read across method and structure activity relationship to evaluate structurally similar compounds that do have data

Gelbke, et al. Toxicological assessment of lower alkyl methacrylate esters by a category approach. Regulatory Toxicology and Pharmacology Volume 92, February 2018, Pages 104-127.

Summary

- Use of human exposure assessment framework on materials selection for wearable technologies
- Overview of dermal health effects related to wearable technologies
- Incorporate various standard methods for biocompatibility evaluation guidelines in wearable technologies